WORLD ANTI-DOPING AGENCY
play true

ISTI, ISL

Athlete Biological Passport Operating Guidelines

Version 6.1

July 2018

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Content

This document is divided into four parts.

Part One provides background and context for the creation of the *ABP*, introduces the Haematological and Steroidal Modules of the Passport and explains the role of the *ABP* Operating Guidelines in supporting *ADOs*.

Part Two describes the Modules and explains the principles for the implementation of the *ABP* by an *ADO*.

Part Three contains Annexes of the *International Standard* for Testing and Investigation (*ISTI*) that incorporate mandatory protocols to be followed by the *ADOs* in connection with Technical Documents for *Laboratories*.

Part Four includes a template agreement developed by *WADA* for the sharing of Passport information between multiple *ADOs* (supported by *ADAMS*).

Part One: Introduction and Objective

1.1 Introduction to the *Athlete Biological Passport*

The term "athlete biological passport" was first proposed in the early 2000s by the scientific community when monitoring of select haematological variables (*Markers* of blood doping) was identified as a means to define an individual's haematological profile. In conjunction with several stakeholders and medical experts, the World Anti-Doping Agency *(WADA)* began to further develop, harmonize and validate this concept. The result was a formal operating guideline and mandatory standards known as the *Athlete Biological Passport* (*ABP*), first published in 2009, which concerned exclusively the haematological module.

In 2014, the initial system was complemented with the Steroidal Module, which was launched in order to establish longitudinal profiles of an *Athlete*'s steroid variables. The framework proposed in these Guidelines builds on existing anti-doping infrastructure to promote harmonization in *ABP* Programs, facilitate exchange of information and mutual recognition of data and, consequently, to enhance efficiencies in the operation of Anti-Doping Activities.

These Guidelines provide a harmonized process for both the Haematological Module and the Steroidal Module of the *ABP*, following nearly identical administrative procedures in *ADAMS*.

As with all Guidelines, this document is subject to ongoing review and assessment to ensure it continues to reflect best practice moving forward. *WADA* encourages feedback on this document and recommends stakeholders to consult *WADA's* Web site, http://www.wada-ama.org for the latest version.

1.2 Objective

The principle objectives of integrating the *ABP* into the larger framework of a robust anti-doping program are the following:

1. The *ABP* can be used to identify *Athletes* for specific *Target Testing* through intelligent, timely interpretation of Passport data. The *ABP* provides valuable information that can be used to direct *Target Testing* or investigations more effectively. The *ABP* can notably be used as a complement to analytical methods to further refine and strengthen overall anti-doping strategies:

   i) For the Haematological Module, this could be, for example, *Testing* for Erythropoiesis-Stimulating Agents (ESAs) or homologous blood transfusion (HBT).

   ii) For the Steroidal Module, this could be, for example, the use of Gas Chromatography-Combustion-Isotope Ratio Mass Spectrometry (GC-C-IRMS) to detect endogenous steroids administered exogenously.

2. A Passport may be used to pursue an Anti Doping Rule Violation (ADRV) in accordance with World Anti-Doping Code (*Code*) Article 2.2. Through changes in biological *Markers* of doping collated over an *Athlete*'s career, the *ABP* can be used to establish '*Use'* per *Code* article 2.2 without necessarily relying on the detection of a particular *Prohibited Substance* or *Prohibited Method*. This approach has proven effective in establishing ADRVs without having to rely on traditional analytical approaches.

Part Two: Modules, Management and Administration

2.1 Modules

2.1.1 Haematological Module

The Haematological Module collects information on *Markers* of blood doping. This Module aims to identify the *Use* of *Prohibited Substances* and/or *Prohibited Methods* for the enhancement of oxygen transport or delivery, including the *Use* of ESAs and any form of blood transfusion or manipulation.

In addition to identifying the use of ESAs included under section S2 of the *Prohibited List* (Peptide Hormones, Growth Factors, Related Substances and Mimetics), the Haematological Module also seeks to identify the *Use of Prohibited Methods* categorized under section M1 of the *Prohibited List* (Manipulation of Blood and Blood Components).

The following *Markers* are considered within the *ABP* Haematological Module:

HCT:	Haematocrit
HGB:	Haemoglobin
RBC:	Red blood cell (erythrocyte) count
RET%:	Reticulocytes percentage
RET#:	Reticulocyte count
MCV:	Mean corpuscular volume
MCH:	Mean corpuscular haemoglobin
MCHC:	Mean corpuscular haemoglobin concentration
RDW-SD:	Red cell distribution width (standard deviation)
IRF:	Immature reticulocyte fraction
OFFS:	OFF-hr Score
ABPS:	Abnormal Blood Profile Score (ABPS)

2.1.2 Steroidal Module

The Steroidal Module collects information on *Markers* of steroid doping. The Module aims to identify endogenous anabolic androgenic steroids (EAAS) when administered exogenously and other anabolic agents, such as selective androgen receptor modulators (SARMS) categorized under Section S1.2 of the *Prohibited List*. The Steroidal Module is also an effective means to identify samples which may have been tampered with or exchanged with the urine of another person (*Code* article 2.5).

The following *Markers* are considered within the *ABP* Steroidal Module (the "steroid profile"), as detailed in the Technical Document on Endogenous Anabolic Androgenic Steroids Measurement and Reporting (see Section 3.3 below):

- testosterone (T);
- epitestosterone (E);
- androsterone (A);
- etiocholanolone (Etio);
- 5α-androstane-3α,17β-diol (5αAdiol);
- 5β-androstane-3α,17β-diol (5βAdiol);

and the following ratios:

- testosterone to epitestosterone (T/E);
- androsterone to testosterone (A/T);
- androsterone to etiocholanolone (A/Etio);
- 5α-androstane-3α,17β-diol to 5β-androstane-3α,17β-diol (5αAdiol/5βAdiol); and
- 5α-androstane-3α,17β-diol to epitestosterone (5αAdiol/E).

2.2 Resources, Partner Roles and Responsibilities

The roles and responsibilities of the various partners implementing the *ABP* include test planning, conducting the sample collection, profile interpretation and results management.

2.2.1 Resources

The following resources are required to adopt and implement the *ABP*:

- Access to a network of *Doping Control* Officers (DCOs) and Blood Collection Officers (BCOs) where necessary, operating in locations where target *Athletes* will be present.
- An effective whereabouts management system to facilitate *Athlete* location (i.e. *ADAMS*).

- Access to *ADAMS*, to administer the *ABP* Program.
- An APMU, associated with a *WADA* accredited *Laboratory* or an *APMU* internal to the *ADO,* with relevant expertise and availability for "real-time" management of *ABP* processes.
- An Expert panel with appropriate interpretive and consultative skills associated to the APMU. The Experts are appointed by the *ADO* in consultation with the APMU.

[2.3.2 Comments: Access to the ADAMS Biological Passport Guide is available at the following link:
http://adams-docs.wada-ama.org/display/EN/ADAMS+Biological+Passport+guide]

2.2.2 Specific Partner Responsibilities

2.2.2.1 *Anti-Doping Organization*

The *ADO* is responsible for:

- Adopting, implementing and administrating an *ABP* program in accordance with these Guidelines, including compliance with the *ISTI*.
- Establishing an internal or external APMU to manage the *ABP* program.
- Ensuring that recommendations received from the APMU are followed by effective, targeted, timely and appropriate *Testing*.
- Establishing, and implementing a test distribution plan, in consultation with the APMU.
- Sharing of relevant information with internal investigations personel and other *ADOs* (when appropriate).
- When the *ADO* is the *Passport Custodian*, following up on *Adverse Passport Findings* (*APFs*) in accordance with *Code* and ISTI requirements.
- Informing the *Athlete* in case the Passport indicates a likely pathology as determined by the Experts.

2.2.2.2 Athlete Passport Management Unit (APMU)

The APMU is responsible for:

- Timely management of the Passports in *ADAMS*.
- Assessing sample validity and supporting documentation, in consultation with the Experts or *Laboratories* when necessary.
- Issuing and updating the APMU Reports in *ADAMS*, which may provide follow up recommendations as described below in Section 2.3.4.
- In case of an *ATPF,* or when a review is otherwise justified, liaising with the Expert panel as required in Annex L - *ISTI* (Section 3.4 below).

- Compiling all necessary information to establish an *ABP* Documentation Package.
- Declaring *Adverse Passport Findings* (*APFs)* to the *Passport* Custodian and *WADA*.
- Providing the Experts from time to time with Passports for review, even when the values are within normal limits and presenting no suspicious elements as this will ensure that Experts are provided a balanced perspective on the *Athletes* Passports.
- Defining or proposing priorities to the *ADO* in order to optimize the efficiency of the whole *ABP* program, including cost efficiency.

2.2.2.3 *Laboratory*

The *WADA*-accredited *Laboratory* or *WADA*-Approved Laboratory for the *ABP* is responsible for:

- Blood analysis: perform blood analysis in compliance with the Technical Document on Blood Analytical Requirements for the Athlete Biological Passport (Section 3.2 below).
- Urine analysis: perform urine analysis in compliance with the Technical Document on Endogenous Anabolic Androgenic Steroids Measurement and Reporting (Section 3.3 below) for the measurement and reporting of urinary steroid profiles.
- Issuing a Certificate of Analysis or Laboratory Documentation Package as applicable.
- Providing additional information for interpretation of results and for complementary analysis.

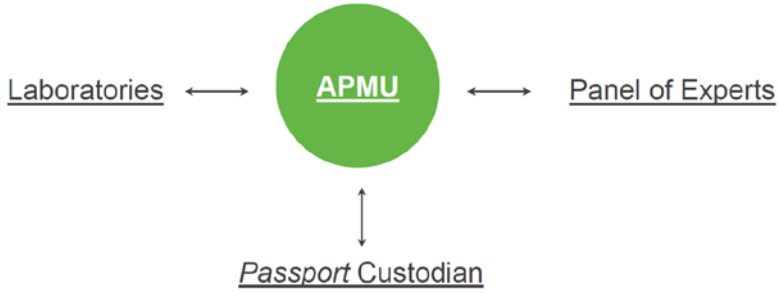
2.2.2.4 Experts

The Experts are responsible for:

- Reviewing Passport data and results from the Adaptive Model in ADAMS provided by the APMU. The review shall identify any possible pathological or confounding conditions that may have impacted an Athlete's analytical results.
- Recommending follow-up Testing and/or suggesting possible clinical Testing that may be required to a) confirm the assessment or b) collect further evidence to support or confirm possible pathologies.
- Reviewing any explanations given by the Athlete and providing an opinion on whether the Passport was likely the result of the Use of a Prohibited Substance or Prohibited Method.
- Working with the relevant APMU as required, and providing support as necessary throughout the results management and hearing process.

2.3 *ABP* Management and Administration

An *ABP* program is administered and managed by an APMU on behalf of, or within, the *ADO*. The APMU is the link between the *Passport* Custodian, the Laboratories, and the Expert panel. Within each Passport in *ADAMS*, the APMU Report provides a record of these various interactions for efficient follow-up by the *Passport* Custodian, WADA and other *ADOs* with whom the Passport is shared though ADAMS.



2.3.1 *Testing* and Defining the Target *Athletes*

An *ABP Testing* Program must follow the *ISTI* and applicable TDs specific to the *ABP* (Part Three below).

Targeted tests that follow the recommendations of the APMU should be privileged over Random Selection *Testing* to improve the effectiveness of the *ABP*. In general, the effectiveness of the *ABP* to detect doping is improved where both *In-* and *Out-of Competition Testing* and No Advance Notice *Testing* are distributed strategically throughout the year.

[2.1 Comment: For the Haematological Module, it is recommended to use data from samples collected 5 days apart or more to optimize the statistical significance of the data. This does not preclude Testing an Athlete less than five (5) days apart, notably and without limitation, when a potential risk of doping practices has been identified. The validity of the Samples and their inclusion in the Expert review is in any event not put in question by the collection frequency.]
Without limitation, the criteria listed in ISTI Article 4.2 are the factors that may be considered in determining the target population for the ABP in the context of an ADO's overall Test Distribution Plan (TDP).

2.3.2 *Athlete* Information

Given that additional information is required from *Athletes* beyond what is collected in traditional *Doping Control* documentation pursuant to the *ISTI*, supplemental or revised documentation may be required. Such documentation may be collected as appropriate, both prior to and after *Testing*, for APMU assessment and Experts review as required.

For *ABP* blood *Samples*, in addition to the mandatory information set out in *ISTI* Article 7.4.5, which must be recorded as a part of all *Sample* Collection Sessions, the information listed in *ISTI* K.2.6 (Section 3.1 below) shall be recorded in a specific *ABP* Supplementary Form or a related form to be signed by the *Athlete*.

See the available *ABP* Supplementary Form template:

https://www.wada-ama.org/en/resources/world-anti-doping-program/athlete-biological-passport-supplementary-report-form

2.3.3 Standardization through *ADAMS*

The *ABP* Program is administered through *WADA's Anti-Doping Administration and Management System (ADAMS),* a secure online database management tool for data entry, storage, sharing, and reporting, designed to assist stakeholders and *WADA* in their anti-doping operations. An essential element of the *ABP*, the Adaptive Model, is fully integrated into *ADAMS*. Only programs that fully utilize *ADAMS* can be considered *ABP* Programs.

Standardization and harmonization of *ABP* programs is achieved through the use of *ADAMS*. This ensures that all mandatory requirements are met and that the *Athlete* Passports are shared and stored securely, all in accordance with the *International Standard* for the Protection of Privacy and Personal Information (ISPPPI). Furthermore, *ADAMS* facilitates prompt exchange of information between *ADOs*, APMUs, Laboratories and/or *WADA*-Approved Laboratories for the *ABP*, *Sample* Collection Personnel, and *WADA*.

2.3.4 APMU Report

The APMU Report is a central element in the administrative sequence of the *ABP* that is entered and maintained by the APMU in *ADAMS.* It provides an up to date overview of the current status of an *Athlete's* Passport together with recommendations, as appropriate, for efficient follow-up by the *Passport* Custodian. The APMU Report serves to update the *Passport Custodian, WADA* and other *ADOs* with whom the Passport is shared. In addition, it provides a record of events associated with a Passport in *ADAMS*.

The APMU report may include, without limitations:

- Assessments of sample validity by the APMU and/or Experts;
- Recommendations for complementary Analytical Testing (EPO, HIF stabilizers, confirmation of steroid profile, GC-C-IRMS, long-term steroid metabolites, IGF-1, etc.) on Samples collected;
- Recommendations for further Analytical Testing on Samples collected previously;

- Recommendations for storing of Samples for extended periods of time for further analysis;
- Target Testing recommendations based on available data and Experts recommendations;
- A summary of any recent Expert reviews.

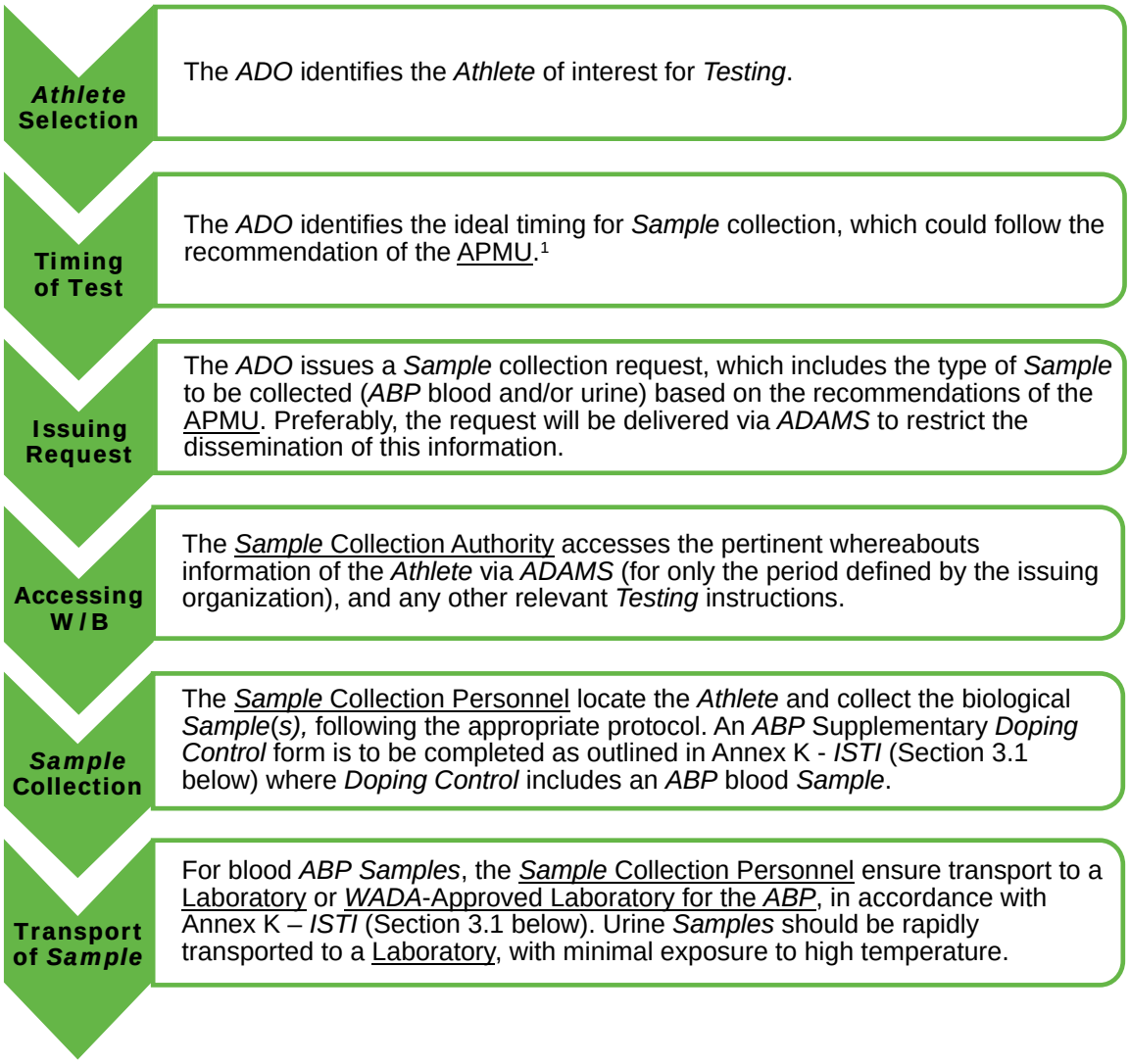
2.3.5 Recommended Administrative Sequence

The following outlines the suggested sequence of interactions between the *Athlete, Sample* Collection Personnel*, ADOs,* Laboratory(ies)*, ADAMS,* APMUs, and Expert panels to establish, follow up and review an individual *Athlete*'s Passport in an effective and efficient manner.

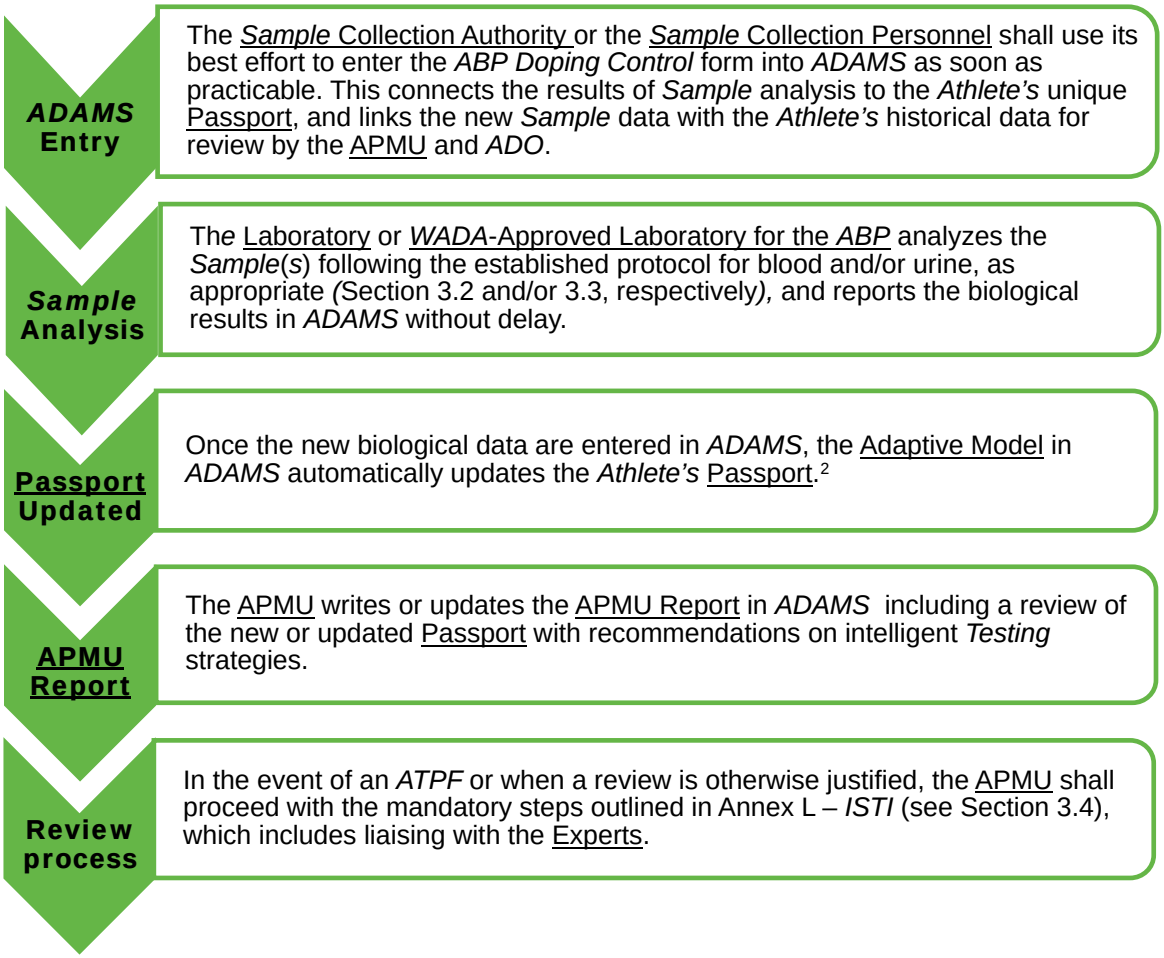
The recommended administrative sequence outlined below may be modified or adapted to merge with existing anti-doping infrastructure, procedures and mechanisms as required. However these Guidelines aim to ensure that *ADOs* establish a process that demonstrates transparency in the planning, interpretation and results management aspects of an *ABP*.

The sequence set out herein includes the incorporation of an APMU that is the central hub connecting Laboratory generated biological data with both the active test planning and intelligence capabilities of the *ADO* and the Expert panel, as required. This APMU may be associated with a *Laboratory*'s operations, or be managed under the responsibility of an *ADO.* The key element of an APMU is that it requires a *Person* or *Persons* with expertise to manage Passports, including recommending further *Testing*, seeking Expert input and coordinating communication.

2.3.6 ABP Administrative Sequence Graphic



BP Administrative Sequence Graphic, *cont.*



[1] When an *ABP* blood *Sample* is collected, the *ADO* must consider whether the collection of concominant urine or blood *Sample*s is warranted, under the circumstances, to perform traditional analysis. For *Out-of-Competition Testing*, it is recommended to collect urine *Samples* together with the blood *Sample*(s) in order to permit Analytical Testing for ESAs when required.

[2] For the Steroidal Module, where the Adaptive Model identifies an *ATPF* for elevated T/E, the *Laboratory* shall proceed with a Confirmation Procedure including GC-C-IRMS analysis. If the *Laboratory* receives a "Suspicious Steroid Profile Confirmation Procedure Request," the *Laboratory* shall proceed with the Confirmation Procedure(s), including the GC-C-IRMS analysis, unless, after contacting the *Testing* Authority, the *Testing* Authority can justify within 7 calendar days that the *Confirmation Procedure(s)* is/are not necessary (see TD2016EAAS, Section 3.3 below, and Annex L – *ISTI*, Section 3.4 below).

2.4 Passport Custody and Passport Sharing

For any individual *Athlete,* only one Passport should be established. Using *ADAMS* for the management of Passport information, *ADOs* enhance efficiencies and program effectiveness through exchange of information and mutual recognition of program outcomes. Such coordination and reciprocal agreement reduces unnecessary duplication in resource expenditure and fosters enhanced confidence among *ADO*s and *Athletes* alike.

All biological results obtained for a same *Athlete* are collated in his Passport regardless of the *Testing* Authority. Only a complete *Athlete's* Passport allows the correct determination of *Atypical Passport Findings* in *ADAMS*. Passport administration and possible Results Management can then follow in compliance with the *Code* with the assurance that the Passports are complete. *ADOs* that fail to share Passport data via *ADAMS* do not operate an *ABP* program.

Within the framework provided by the ISPPPI*, ADOs* are encouraged to coordinate their activities where multiple *ADOs* have *Testing* jurisdiction over a single *Athlete* and multiple *ADO*s may wish to perform Passport *Testing*. In the interests of a "one *Athlete* – one Passport" principle, *ADOs* should work cooperatively to see that *Testing* is coordinated appropriately with all results collated in the *Athlete*'s Passport in *ADAMS*.

Any individual *Athlete* has a *Passport* Custodian that ensures that all *ADOs* that have *Testing* jurisdiction over the *Athlete* do not work in isolation. The *Passport* Custodian is responsible for sharing Passport information with other *ADOs* to ensure proper coordination and best use of resource expenditure. *WADA* has developed a template agreement for the sharing of Passport information between multiple *ADOs* (supported by *ADAMS*), which is included herein in Part Four.

In the case of an *ATPF*, or when a review is otherwise justified, the *Passport* Custodian is responsible for initiating the Passport review process via its APMU and, if an *APF* is declared, for results management of the Passport in compliance with Annex L - *ISTI* (Section 3.4 below), regardless of whether another *ADO* was the *Testing* Authority of the test that triggered the *ATPF*.

In *ADAMS*, Passport custody is attributed to the *Testing* Authority that first tests the *Athlete*, independently of whether it is an *ABP* haematological or steroid test or both. This process ensures that the custody will most likely automatically be assigned to the organization that has a real interest in the *Athlete*.* Passport custody can be transferred to another *ADO* with *Testing* jurisdiction over the *Athlete*.**

* When the *Athlete* is first tested by a *Major Event Organizer* (*MEO*), Passport custody is attributed to the *IF*. When a *NADO* first tests an *Athlete* with a different sport nationality, Passport custody is attributed to the *IF*. This can later be reassigned to another *NADO* if appropriate.

** If no agreement can be found on the Passport custody, *WADA* shall determine which *ADO* is the *Athlete's Passport* Custodian. *WADA* shall not rule on this without consulting the *ADOs* involved.

2.5 Definitions

This document includes defined terms from the *Code*, and these *International Standards* (*IS*): ISTI, ISL and ISPPPI. Code terms are written in italics. *IS* terms are underlined.

2.5.1 2015 *Code* Defined Terms

***ADAMS*:** The Anti-Doping Administration and Management System is a Web-based database management tool for data entry, storage, sharing, and reporting designed to assist stakeholders and *WADA* in their anti-Doping operations in conjunction with data protection legislation.

***Administration*:** Providing, supplying, supervising, facilitating, or otherwise participating in the *Use* or *Attempted Use* by another *Person* of a *Prohibited Substance* or *Prohibited Method*. However, this definition shall not include the actions of bona fide medical personnel involving a *Prohibited Substance* or *Prohibited Method* used for genuine and legal therapeutic purposes or other acceptable justification and shall not include actions involving *Prohibited Substances* which are not prohibited in *Out-of-Competition Testing* unless the circumstances as a whole demonstrate that such *Prohibited Substances* are not intended for genuine and legal therapeutic purposes or are intended to enhance sport performance.

***Adverse Analytical Finding* (*AAF*):** A report from a *WADA*-accredited laboratory or other *WADA*-approved laboratory that, consistent with the International Standard for Laboratories and related Technical Documents, identifies in a *Sample* the presence of a *Prohibited Substance* or its *Metabolites* or *Markers* (including elevated quantities of endogenous substances) or evidence of the *Use* of a *Prohibited Method*.

***Adverse Passport Finding* (*APF*):** A report identified as an *Adverse Passport Finding* as described in the applicable *International Standards*

***Anti-Doping Organization* (*ADO*):** A *Signatory* that is responsible for adopting rules for initiating, implementing or enforcing any part of the *Doping Control* process. This includes, for example, the International Olympic Committee, the International Paralympic Committee, other *Major Event Organizations* that conduct *Testing* at their *Events*, *WADA*, International Federations, and *National Anti-Doping Organizations.*

***Athlete*:** Any *Person* who competes in sport at the international level (as defined by each International Federation) or the national level (as defined by each *National Anti-Doping Organization).* An *Anti-Doping Organization* has discretion to apply anti-doping rules to an *Athlete* who is neither an *International-Level Athlete* nor a *National-Level Athlete*, and thus to bring them within the definition of "Athlete." In

relation to *Athletes* who are neither *International-Level* nor *National-Level Athletes*, an *Anti-Doping Organization* may elect to: conduct limited *Testing* or no *Testing* at all; analyze *Samples* for less than the full menu of *Prohibited Substances*; require limited or no whereabouts information; or not require advance *TUEs*. However, if an Article 2.1, 2.3 or 2.5 anti-doping rule violation is committed by any *Athlete* over whom an *Anti-Doping Organization* has authority who competes below the international or national level, then the *Consequences* set forth in the *Code* (except Article 14.3.2) must be applied. For purposes of Article 2.8 and Article 2.9 and for purposes of anti-doping information and education, any *Person* who participates in sport under the authority of any *Signatory*, government, or other sports organization accepting the *Code* is an *Athlete*.

[Comment to Athlete: This definition makes it clear that all International- and National-Level Athletes are subject to the anti-doping rules of the Code, with the precise definitions of international- and national-level sport to be set forth in the anti-doping rules of the International Federations and National Anti-Doping Organizations, respectively. The definition also allows each National Anti-Doping Organization, if it chooses to do so, to expand its anti-doping program beyond International- or National-Level Athletes to competitors at lower levels of Competition or to individuals who engage in fitness activities but do not compete at all. Thus, a National Anti-Doping Organization could, for example, elect to test recreational-level competitors but not require advance TUEs. But an anti-doping rule violation involving an Adverse Analytical Finding or Tampering results in all of the Consequences provided for in the Code (with the exception of Article 14.3.2). The decision on whether Consequences apply to recreational-level Athletes who engage in fitness activities but never compete is left to the National Anti-Doping Organization. In the same manner, a Major Event Organization holding an Event only for masters-level competitors could elect to test the competitors but not analyze Samples for the full menu of Prohibited Substances. Competitors at all levels of Competition should receive the benefit of anti-doping information and education.]

***Athlete Biological Passport* (*ABP*):** The program and methods of gathering and collating data as described in the International Standard for Testing and Investigations and International Standard for Laboratories.

***Atypical Finding* (*ATF*):** A report from a *WADA*-accredited laboratory or other *WADA*-approved laboratory which requires further investigation as provided by the International Standard for Laboratories or related Technical Documents prior to the determination of an *Adverse Analytical Finding.*

***Atypical Passport Finding* (*ATPF*):** A report described as an *Atypical Passport Finding* as described in the applicable *International Standards*.

***CAS*:** The Court of Arbitration for Sport.

***Code*:** The World Anti-Doping Code.

***Competition*:** A single race, match, game or singular sport contest. For example, a basketball game or the finals of the Olympic 100-meter race in athletics. For stage races and other sport contests where prizes are awarded on a daily or other interim basis the distinction between a *Competition* and an *Event* will be as provided in the rules of the applicable International Federation.

***Consequences of Anti-Doping Rule Violations* (*Consequences*):** An *Athlete's* or other *Person's* violation of an anti-doping rule may result in one or more of the following: (a) *Disqualification* means the *Athlete's* results in a particular *Competition* or *Event* are invalidated, with all resulting *Consequences* including forfeiture of any medals, points and prizes; (b) *Ineligibility* means the *Athlete* or other *Person* is barred on account of an anti-doping rule violation for a specified period of time from participating in any *Competition* or other activity or funding as provided in Article 10.12.1; (c) *Provisional Suspension* means the *Athlete* or other *Person* is barred temporarily from participating in any *Competition* or activity prior to the final decision at a hearing conducted under Article 8; (d) *Financial Consequences* means a financial sanction imposed for an anti-doping rule violation or to recover costs associated with an anti-doping rule violation; and (e) *Public Disclosure* or *Public Reporting* means the dissemination or distribution of information to the general public or *Persons* beyond those *Persons* entitled to earlier notification in accordance with Article 14. Teams in *Team Sports* may also be subject to *Consequences* as provided in Article 11.

***Doping Control*:** All steps and processes from test distribution planning through to ultimate disposition of any appeal including all steps and processes in between such as provision of whereabouts information, *Sample* collection and handling, laboratory analysis, *TUEs*, results management and hearings.

***Event*:** A series of individual *Competitions* conducted together under one ruling body (e.g., the Olympic Games, FINA World Championships, or Pan American Games).

***In-Competition*:** Unless provided otherwise in the rules of an International Federation or the ruling body of the *Event* in question, "*In-Competition"* means the period commencing twelve hours before a *Competition* in which the *Athlete* is scheduled to participate through the end of such *Competition* and the *Sample* collection process related to such *Competition*.

[Comment to In-Competition: An International Federation or ruling body for an Event may establish an "In-Competition" period that is different than the Event Period.]

***International Event*:** An *Event* or *Competition* where the International Olympic Committee, the International Paralympic Committee, an International Federation, a *Major Event Organization,* or another international sport organization is the ruling body for the *Event* or appoints the technical officials for the *Event.*

***International-Level Athlete*:** *Athletes* who compete in sport at the international level, as defined by each International Federation, consistent with the International Standard for Testing and Investigations.

[Comment to International-Level Athlete: Consistent with the International Standard for Testing and Investigations, the International Federation is free to determine the criteria it will use to classify Athletes as International-Level Athletes, e.g., by ranking, by participation in particular International Events, by type of license, etc. However, it must publish those criteria in clear and concise form, so that Athletes are able to ascertain quickly and easily when they will become classified as International-Level Athletes. For example, if the criteria include participation in certain International Events, then the International Federation must publish a list of those International Events.]

***International Standard*:** A standard adopted by *WADA* in support of the *Code*. Compliance with an *International Standard* (as opposed to another alternative standard, practice or procedure) shall be sufficient to conclude that the procedures addressed by the *International Standard* were performed properly. *International Standards* shall include any Technical Documents issued pursuant to the *International Standard.*

***Major Event Organizations* (*MEOs*):** The continental associations of *National Olympic Committees* and other international multi-sport organizations that function as the ruling body for any continental, regional or other *International Event*.

***Marker*:** A compound, group of compounds or biological variable(s) that indicates the *Use* of a *Prohibited Substance* or *Prohibited Method.*

***Metabolite*:** Any substance produced by a biotransformation process.

***National Anti-Doping Organization* (*NADO*):** The entity(ies) designated by each country as possessing the primary authority and responsibility to adopt and implement anti-doping rules, direct the collection of *Sample*s, the management of test results, and the conduct of hearings at the national level. If this designation has not been made by the competent public authority(ies), the entity shall be the country's *National Olympic Committee* or its designee.

***National Event*:** A sport *Event* or *Competition* involving *International*- or *National-Level Athletes* that is not an *International Event*.

***National-Level Athlete*:** *Athletes* who compete in sport at the national level, as defined by each *National Anti-Doping Organization*, consistent with the International Standard for Testing and Investigations.

***National Olympic Committee* (*NOC*):** The organization recognized by the International Olympic Committee. The term *National Olympic Committee* shall also include the National Sport Confederation in those countries where the National Sport

Confederation assumes typical *National Olympic Committee* responsibilities in the anti-doping area.

***Out-of-Competition*:** Any period which is not *In-Competition*.

***Person*:** A natural *Person* or an organization or other entity.

***Prohibited List*:** The List identifying the *Prohibited Substances* and *Prohibited Methods*.

***Prohibited Method*:** Any method so described on the *Prohibited List*.

***Prohibited Substance*:** Any substance, or class of substances, so described on the *Prohibited List*.

***Registered Testing Pool* (*RTP*):** The pool of highest-priority *Athletes* established separately at the international level by International Federations and at the national level by *National Anti-Doping Organizations,* who are subject to focused *In-Competition* and *Out-of-Competition Testing* as part of that International Federation's or *National Anti-Doping Organization*'s test distribution plan and therefore are required to provide whereabouts information as provided in Article 5.6 and the International Standard for Testing and Investigations.

***Sample or Specimen*:** Any biological material collected for the purposes of *Doping Control*.

[Comment to Sample or Specimen: It has sometimes been claimed that the collection of blood Samples violates the tenets of certain religious or cultural groups. It has been determined that there is no basis for any such claim.]

***Tampering*:** Altering for an improper purpose or in an improper way; bringing improper influence to bear; interfering improperly; obstructing, misleading or engaging in any fraudulent conduct to alter results or prevent normal procedures from occurring.

***Target Testing*:** Selection of specific *Athletes* for *Testing* based on criteria set forth in the International Standard for Testing and Investigations.

***Testing*:** The parts of the *Doping Control* process involving test distribution planning, *Sample* collection, *Sample* handling, and *Sample* transport to the laboratory.

***Use*:** The utilization, application, ingestion, injection or consumption by any means whatsoever of any *Prohibited Substance* or *Prohibited Method*.

***WADA*:** The World Anti-Doping Agency.

2.5.2 *ISTI* Defined Terms

Blood Collection Officer (BCO): An official who is qualified to and has been authorized by the *Sample* Collection Authority to collect a Blood *Sample* from an *Athlete*.

Chain of Custody: The sequence of individuals or organizations who have responsibility for the custody of a *Sample* from the provision of the *Sample* until the *Sample* has been delivered to the laboratory for analysis.

***Doping Control* Officer (DCO):** An official who has been trained and authorized by the *Sample* Collection Authority to carry out the responsibilities given to DCOs in the International Standard for Testing and Investigations.

***Doping Control* Station:** The location where the *Sample* Collection Session will be conducted.

No Advance Notice *Testing*: *Sample* collection that takes place with no advance warning to the *Athlete* and where the *Athlete* is continuously chaperoned from the moment of notification through *Sample* provision.

Random Selection: Selection of *Athletes* for *Testing* which is not *Target Testing*.

***Sample* Collection Authority:** The organisation that is responsible for the collection of *Samples* in compliance with the requirements of the International Standard for Testing and Investigations, whether (1) the *Testing* Authority itself; or (2) another organization (for example, a third party contractor) to whom the *Testing* Authority has delegated or sub-contracted such responsibility (provided that the *Testing* Authority always remains ultimately responsible under the *Code* for compliance with the requirements of the International Standard for Testing and Investigations relating to collection of *Samples*).

***Sample* Collection Equipment:** Containers or apparatus used to collect or hold the *Sample* at any time during the *Sample* Collection Session. *Sample* Collection Equipment shall, as a minimum, consist of:

- For urine *Sample* collection:
    - Collection vessels for collecting the *Sample* as it leaves the *Athlete's* body;
    - Suitable kit for storing partial *Samples* securely until the *Athlete* is able to provide more urine; and
    - Sealable and tamper-evident bottles and lids for storing and transporting the complete *Sample* securely.
- For blood *Sample* collection:
    - Needles for collecting the *Sample*;

- Blood tubes with sealable and tamper-evident devices for storing and transporting the *Sample* securely.

***Sample* Collection Personnel:** A collective term for qualified officials authorized by the *Sample* Collection Authority to carry out or assist with duties during the *Sample* Collection Session.

***Sample* Collection Session:** All of the sequential activities that directly involve the *Athlete* from the point that initial contact is made until the *Athlete* leaves the *Doping Control* Station after having provided his/her *Sample(s)*.

Test Distribution Plan (TDP): A document written by an *Anti-Doping Organization* that plans *Testing* on *Athletes* over whom it has *Testing* Authority, in accordance with the requirements of Article 4 of the International Standard for Testing and Investigations.

***Testing* Authority:** The organization that has authorized a particular *Sample* collection, whether (1) an *Anti-Doping Organization* (for example, the International Olympic Committee or other *Major Event Organization*, *WADA*, an International Federation, or a *National Anti-Doping Organization*); or (2) another organization conducting *Testing* pursuant to the authority of and in accordance with the rules of the *Anti-Doping Organization* (for example, a National Federation that is a member of an International Federation).

2.5.3 ISL Defined Terms

Adaptive Model: A mathematical model that was designed to identify unusual longitudinal results from *Athletes*. The model calculates the probability of a longitudinal profile of *Marker* values assuming that the *Athlete* has a normal physiological condition.

Aliquot: A portion of the *Sample* of biological fluid or tissue (e.g. urine, blood) obtained from the *Athlete* used in the analytical process.

Analytical Testing: The parts of the *Doping Control* process involving *Sample* handling, analysis and reporting following receipt in the Laboratory.

***Athlete Passport* Management Unit (APMU):** A unit composed of a *Person* or *Persons*, designated by the *Anti-Doping Organization*, responsible for the administrative management of the Passports in *ADAMS*, advising the *Anti-Doping Organization* for intelligent, *Targeted Testing* through the APMU report, liaising with the Expert panel, compiling and authorizing an *Athlete Biological Passport* Documentation Package and reporting *Adverse Passport Findings*.

Confirmation Procedure: An analytical test procedure whose purpose is to identify the presence or to measure the concentration/ratio of one or more specific *Prohibited*

Substances, *Metabolite*(*s*) of a *Prohibited Substance*, or *Marker*(*s*) of the *Use* of a *Prohibited Substance* or *Method* in a *Sample*.

[Comment: A Confirmation Procedure for a threshold substance shall also indicate a concentration/ratio of the Prohibited Substance greater than the applicable Decision Limit (as noted in the TD DL).]

Initial *Testing* Procedure: An analytical test procedure whose purpose is to identify those *Samples* which may contain a *Prohibited Substance*, *Metabolite*(*s*) of a *Prohibited Substance*, or *Marker*(*s*) of the *Use* of a *Prohibited Substance* or *Prohibited Method* or the quantity of a *Prohibited Substance*, *Metabolite*(*s*) of a *Prohibited Substance*, or *Marker*(*s*) of the *Use* of a *Prohibited Substance* or *Prohibited Method*.

International Standard for Laboratories (ISL): The International Standard applicable to Laboratories as set forth herein.

Laboratory(ies): *WADA*-accredited laboratory(ies) applying test methods and processes to provide evidentiary data for the detection of *Prohibited Substances*, *Methods* or *Markers* on the *Prohibited List* and, if applicable, quantification of a Threshold Substance in *Samples* of urine and other biological matrices in the context of anti-doping activities.

Laboratory Documentation Packages: The material produced by the Laboratory to support an analytical result such as an *Adverse Analytical Finding* as set forth in the *WADA* Technical Document for Laboratory Documentation Packages.

***WADA*-Approved Laboratory for the *ABP*:** Laboratory(ies) not otherwise accredited by *WADA*; applying test methods and processes in support of an *Athlete Biological Passport* program and in accordance with the criteria for approval of non-accredited laboratories for the *Athlete Biological Passport*.

2.5.4 ISPPPI Defined Terms

Anti-Doping Activities: Activities specified by the *Code* and the *International Standards* to be carried out by *Anti-Doping Organizations*, and their Third-Party Agents, for the purpose of establishing whether anti-doping rule violations took place, including collecting whereabouts information; conducting *Testing*; performing results management; determining whether an *Athlete's Use* of a *Prohibited Substance* or *Prohibited Method* is strictly limited to legitimate and documented therapeutic purposes; educating *Participants* on their rights and responsibilities; conducting investigations into anti-doping rule violations; and initiating legal proceedings against those who are alleged to have committed such a violation.

Personal Information: Information, including without limitation Sensitive Personal Information, relating to an identified or identifiable *Participant* or relating to other *Persons* whose information is Processed solely in the context of an *Anti-Doping Organization's* Anti-Doping Activities.

[3.2 Comment: It is understood that Personal Information includes, but is not limited to, information relating to an Athlete's name, date of birth, contact details and sporting affiliations, whereabouts, designated therapeutic use exemptions (if any), anti-doping test results, and results management (including disciplinary hearings, appeals and sanctions). Personal Information also includes personal details and contact information relating to other Persons, such as medical professionals and other Persons working with, treating or assisting an Athlete in the context of Anti-Doping Activities. Such information remains Personal Information and is regulated by this Standard for the entire duration of its Processing, irrespective of whether the relevant individual remains involved in organized sport.]

Processing (and its cognates, Process and Processed): Collecting, retaining, storing, disclosing, transferring, transmitting, amending, deleting or otherwise making use of Personal Information.

Security Breach: Any unauthorized and/or unlawful Processing of, including access to, Personal Information whether in electronic or hard-copy or other form, or interference with an information system, that compromises the privacy, security, confidentiality or integrity of Personal Information.

Third Party: Any natural *Person* or legal entity other than the natural *Person* to whom the relevant Personal Information relates, *Anti-Doping Organizations* and Third-Party Agents.

2.5.5 ABP Operating Guidelines and Related TDs Defined Terms

***Athlete Biological Passport* Documentation Package:** The material produced by the Laboratory and *Athlete Passport* Management Unit to support an *Adverse Passport Finding* such as, but not limited to, analytical data, Expert panel comments, evidence of confounding factors as well as other relevant supporting information.

APMU Report: A report maintained by the *Athlete Passport* Management Unit, available in the *Athlete*'s Passport in *ADAMS*, that provides a comprehensive summary of the Expert(s) review(s) and recommendations for effective and appropriate follow-up *Testing* by the *Passport* Custodian.

Expert: The Expert(s), and/or Expert panel, with knowledge in the concerned field, chosen by the *Anti-Doping Organization* and/or *Athlete Passport* Management Unit, are responsible for providing an evaluation of the Passport. The Expert must be external to the *Anti-Doping Organization*. For the Haematological Module, the Expert should have knowledge in one or more of the fields of clinical haematology (diagnosis of blood pathological conditions), sports medicine and/or exercise physiology. For the Steroidal Module, the Expert should have knowledge in Laboratory analysis, steroid doping and/or endocrinology. For both modules, an Expert panel should consist of Experts with complementary knowledge such that all relevant fields are represented. The Expert panel may include a pool of at least three appointed Experts and any

additional ad hoc Expert(s) who may be required upon request of any of the appointed Experts or by the *Athlete Passport* Management Unit of the *Anti-Doping Organization.*

Passport: A collation in *ADAMS* of all relevant data unique to an individual *Athlete* that include longitudinal profiles of *Markers*, the APMU report, heterogeneous factors unique to that particular *Athlete* and other relevant information that may help in the evaluation of *Markers*.

Passport Custodian: The *Anti-Doping Organization* responsible for result management of that *Athlete*'s Passport and for sharing any relevant information associated to that *Athlete*'s Passport with other *Anti-Doping Organization(s)*.

Part Three: Mandatory Protocols

3.0 Scope

ADOs implementing an *ABP* Program shall follow mandatory protocols documented in Annexes of the *International Standard for Testing and Investigations (*ISTI). Included herein for the ease of reference, these requirements have been established to harmonize the results of monitored biological *Markers* within the *ABP* to ensure both legal fortitude and scientific certainty. This standardization of procedure allows for the sharing and mutual recognition of Passport data between the anti-doping programs of multiple *ADOs*. Only programs that fully adhere to these protocols and fully utilize *ADAMS* can be considered *ABP* Programs. These protocols are linked to Technical Documents (TDs) that a *Laboratory* or Laboratory approved for the *ABP* shall follow for the analysis of *Samples* collected within the framework of the *ABP* (TDs included herein for the sake of completeness).

Section 3.1 sets out the minimum requirements for *Sample* collection and *Sample* transport that an *ADO* shall fulfil to run the Haematological Module of the *ABP* program (Annex K - *ISTI*). Sections 3.2 and 3.3 are TDs intended for *Laboratory* personnel that aim to harmonize the analysis of blood or urine *Samples* collected for the measurement of the *Markers* of the Haematological and Steroidal Modules of the *ABP*. Finally, Section 3.4 sets out the requirements and procedures that the Passport Custodian and its APMU shall follow for Result Management for the *ABP* (Annex L - *ISTI*).

3.1 Collection, Storage and transport of *ABP* blood *Samples* (ISTI Annex K)

K.1 Objective

To collect an *Athlete's* blood *Sample,* intended for use in connection with the measurement of individual *Athlete* blood variables within the framework of the *Athlete Biological Passport* program, in a manner appropriate for such use.

K.2 Requirements

K.2.1 If collection occurs after training or *Competition*, test planning shall consider the *Athlete*'s whereabouts information to ensure *Testing* does not occur within two hours of such activity. If the *Athlete* has trained or competed less than two hours before the time the *Athlete* has been notified of his/her selection, the DCO or other designated *Sample* Collection Personnel shall chaperone the *Athlete* until this two-hour period has elapsed.

If the *Sample* was collected within two hours of training or *Competition*, the nature, duration and intensity of the exertion shall be recorded by the DCO to make this information available to the APMU and subsequently to the Experts.

K.2.2 Although a single blood *Sample* is sufficient within the framework of the *ABP*, it is recommended to collect an additional "B" *Sample* for a possible subsequent analysis of *Prohibited Substances* and *Methods* in whole blood (e.g. detection of Homologous Blood Transfusion (HBT), and/or Erythropoiesis Stimulating Agents (ESAs).

For *Out-of-Competition Testing*, "A" and "B" urine *Samples* should be collected together with the blood *Sample(s)* in order to permit Analytical Testing for ESAs unless otherwise justified by a specific intelligent testing strategy.

[Comment: WADA's Blood Sample Collection Guidelines reflect these protocols and include practical information on the integration of ABP Testing into "traditional" Testing activities. A table has been included within the Blood Sample Collection Guidelines that identifies which particular timelines for delivery are appropriate when combining particular test types (i.e. ABP + Growth Hormone (GH), ABP + HBT, etc.), and which types of Samples may be suited for simultaneous transport.]

K.2.3 The *Sample* shall be refrigerated from its collection until its analysis with the exception of when the *Sample* is analyzed at the collection site without delay. The storage procedure is the DCO's responsibility.

The storage and transport device shall be capable of maintaining blood *Samples* at a cool temperature during storage. Whole blood *Samples* shall not be allowed to freeze

at any time. In choosing the storage and transport device, the DCO shall take into account the time of storage, the number of *Samples* to be stored in the device and the prevailing environmental conditions (hot or cold temperatures). The storage device shall be:

a) Refrigerator.

b) Insulated cool box.

c) Isotherm bag.

d) Any other device that possesses the capabilities mentioned below.

K.2.4 A temperature data logger shall be used to record the temperature from the collection to the analysis of the *Sample* except when the *Sample* is analyzed at the collection site without delay. The temperature data logger shall be able to:

a) record the temperature in degrees Celsius at least once per minute;

b) record time in GMT;

c) report the temperature profile over time in text format with one line per measurement following the format “YYYY-MM-DD HH:MM T”;

d) have a unique ID of at least six characters.

K.2.5 Following notification to the *Athlete* that he/she has been selected for *Doping Control*, and following the DCO/BCO’s explanation of the *Athlete’s* rights and responsibilities in the *Doping Control* process, the DCO/BCO shall ask the *Athlete* to remain in a normal seated position with feet on the floor for at least 10 minutes prior to providing a blood *Sample*.

[Comment: the Athlete shall not stand up at any time during the 10 minutes prior to Sample collection. To have the Athlete seated during 10 minutes in a waiting room and then to call the Athlete into a blood collection room is not acceptable.]

K.2.6 In addition to a regular *Doping Control* form, the DCO/BCO shall use the ABP Supplementary Form if such a form is available. If an *ABP*-specific *Doping Control* form is unavailable, the DCO/BCO shall still use a regular *Doping Control* form but he/she shall collect and record the following additional information on a related form or supplementary report to be signed by the *Athlete* and the DCO/BCO:

a) Confirm that there was no training or *Competition* in the two hours prior to the blood test.

b) Did the *Athlete* train, compete or reside at an altitude greater than 1,500 meters within the prior two weeks? If so, or if in doubt, the name and location of the place where the *Athlete* had been and the duration of his/her stay shall be recorded. The estimated altitude shall be entered, if known.

c) Did the *Athlete* use any form of altitude simulation such as a hypoxic tent, mask, etc. during the prior two weeks? If so, as much information as possible

on the type of device and the manner in which it was used (e.g. frequency, duration, intensity) should be recorded.

d) Did the *Athlete* receive any blood transfusion(s) during the prior three months? Was there any blood loss due to accident, pathology or donation in the prior three months? What was the estimated volume?

e) The DCO/BCO should record on the *Doping Control* form any extreme environmental conditions the *Athlete* was exposed to during the last two hours prior to blood collection, including any sessions in any artificial heat environment, such as a sauna.

f) Was the *Sample* collected immediately following at least three consecutive days of an intensive endurance *Competition*, such as a stage race in cycling?

K.2.7 The DCO/BCO shall start the temperature data logger and place it in the storage device. It is important to start recording the temperature before Sample collection.

The storage device shall be located in *Doping Control* Station and shall be kept secured appropriately in accordance with the *ISTI*.

K.2.8 The DCO/BCO instructs the *Athlete* to select the *Sample* Collection Equipment in accordance with *ISTI* Article E.4.6. If Vaccutainer®(s) are not pre-labelled, the DCO/BCO shall label them with a unique Sample code number prior to the blood being drawn and the Athlete shall check that the code numbers match.

K.3 The *Sample* Collection Procedure

The *Sample* collection procedure for the collection of blood for the purposes of the *ABP* is consistent with the procedure set out in *ISTI* Articles E.4, with the following additional elements:

a) The BCO ensures that the 10-minute (or more) seated period has elapsed prior to performing venipuncture and drawing blood; and

b) The BCO ensures that the vacuum tubes were filled appropriately; and

c) After the blood flow into the tube ceases, the BCO removes the tube from the holder and homogenizes the blood in the tube manually by inverting the tube gently at least three times.

K.3.1 The *Athlete* and the DCO/BCO sign the *Doping Control* and ABP supplementary form(s), when applicable.

The blood *Sample* is sealed and deposited in the storage device next to the temperature data logger.

K.4 Transportation Requirements

Blood *Samples* shall be transported in a device that maintains the integrity of *Samples* over time, due to changes in external temperature.

The transport procedure is the DCO's responsibility. The transport device shall be transported by secure means using an *ADO*-authorized transport method.

K.4.1 The integrity of the *Markers* used in the haematological module of the *ABP* is guaranteed when the Blood Stability Score (BSS) remains below 85, where the BSS is computed as:

BSS = 3 * T + CAT

With « CAT » being the Collection to Analysis Time (in hours), and T the average Temperature (in degrees Celsius) measured by the data logger between *Sample* collection and analysis.

Within the framework of the BSS, the following table can be used by the DCO/BCO to estimate the maximal transport time to a Laboratory or *WADA*- Approved Laboratory for the *ABP*, called the Collection to Reception Time (CRT), for a given average temperature T:

T [°C]	CRT [h]
15	35
12	41
10	46
9	48
8	50
7	53
6	55
5	58
4	60

The DCO/BCO shall apply a conservative approach and rapidly transport the *Sample* to a Laboratory or *WADA*- Approved Laboratory for the *ABP* located close to the *Sample* collection site.

K.4.2 The DCO, BCO or other *Sample* Collection Personnel shall report without delay into ADAMS:

a) The *Doping Control* form;

b) The *ABP* Supplementary form, and/or the additional information specific to the *ABP* collected on a related form or supplementary report;

c) In the Chain of Custody, the temperature data logger ID (without any time reference) and the time zone of the testing location in GMT.

3.2 Blood Analytical Requirements for the *Athlete Biological Passport*

WADA Technical Document – TD2018BAR

Document Number:	TD2018BAR	Version Number:	1.0
Written by:	*WADA*	Approved by:	*WADA* Executive Committee
Date:	16 May 2018	Effective Date:	01 July 2018

Introduction

This Technical Document (TD) has been established to harmonize the analysis of blood *Sample*s collected, both *In-Competition* and *Out-of-Competition*, for the measurement of individual *Athlete* blood *Markers* within the framework of the *Athlete Biological Passport* (*ABP*).

The *International Standard* for Laboratories (ISL) is applicable to the analysis of blood *Sample*s carried out in connection with the measurement of individual *Athlete* blood *Markers* within the framework of the *ABP*. This TD describes certain specificities of blood analysis related to the *ABP*.

To standardize analytical results in the *ABP* framework, blood *Sample*s shall only be analyzed in the dedicated network of Laboratories (i.e. *WADA*-accredited or *WADA*-Approved Laboratories for the *ABP*) which are accredited or approved by WADA to perform the analysis and with analyzers of comparable technical characteristics. The instrumentation and test shall by validated and ISO/IEC (17025 or 15189) accredited and the Laboratories shall participate in the *WADA* External Quality Assessment Scheme (EQAS) for blood samples prior to analysis of *Doping Control Sample*s.

If not reasonably possible for blood *Sample*s to be analyzed in a Laboratory or *WADA*-Approved Laboratory for the *ABP* for technical and/or geographical reasons, blood *Sample*s can be analyzed at a satellite facility of a Laboratory or using mobile units operated under applicable ISO/IEC accreditation (17025 or 15189) by a Laboratory. Satellite facilities and mobile units shall also be validated, ISO/IEC (17025 or 15189) accredited and participate in the *WADA* EQAS for blood samples prior to analysis of *Doping Control Sample*s. *Sample* handling shall be conducted in compliance with the Technical Document on Laboratory Internal Chain of Custody (TD LCOC).

2. Sample Reception and Timing

The blood *Sample* shall be analyzed as soon as possible upon reception and no later than 12 hours of *Sample* reception unless the *Sample* Collection Authority provides specific information regarding the *Sample* collection and transportation conditions which would allow the Laboratory to extend the time window of the analysis of the *Sample* without affecting blood stability.

In cases when the Laboratory or *WADA*-Approved Laboratory for the *ABP* is unable to immediately analyze the *Sample* after reception, the Laboratory or *WADA*-Approved Laboratory for the *ABP* is responsible for maintaining the *Sample* at a cool temperature (approximately 4°C) between reception and the start of the analytical procedure. The temperature data logger shall accompany the *Sample* until Sample homogeneization. The blood *Sample* shall not be aliquoted before analysis[1].

If there is a Laboratory or *WADA*-Approved Laboratory for the *ABP* deviation from the aforementioned procedure, the Laboratory or *WADA*-Approved Laboratory for the *ABP* shall proceed with the analysis and report the results into *ADAMS* with a detailed description of the deviation.

3. Instrument Check

Before performing any blood analyses, all reagents must be verified to ensure that they are within their expiration dates, and that they comply with the reagent manufacturer's recommendations. Operational parameters of the instrument must be properly controlled (background level, temperature of the incubation chambers, pressure, etc.) and fall within the manufacturer's specifications.

All internal quality controls (levels 1, 2 and 3) shall be analyzed twice consecutively following the specifications provided by the manufacturer prior to the analysis of *Samples*. All results shall be in agreement with the reference value ranges provided by the manufacturer. These internal quality controls shall be furnished exclusively by the manufacturer of the instrument and handled in strict accordance with the specifications provided by the manufacturer (e.g. expiration dates, storage conditions). The internal quality controls shall be monitored via quality control charts with appropriate control limits.

At least one internal quality control from the manufacturer (either level 1, 2 or 3) shall be analyzed after every 30 to 50 blood *Samples*. At the end of each analysis session and after all blood *Sample* analyses are completed, one internal quality control (either level 1, 2 or 3) shall be analyzed once again to demonstrate the continuous stability of the instrument and the quality of the analyses done.

[1] It is possible to aliquot the *Sample* after analysis for the *ABP*, when appropriate.

On a regular basis (as determined by the head of the Laboratory or *WADA*-Approved Laboratory for the *ABP*), one fresh blood *Sample* shall be homogenized for a minimum period of 15 minutes on an appropriate mixer (e.g. roller mixer) and then analyzed seven consecutive times. Coefficients of variation shall be below 1.5% for Haemoglobin (HGB) and Haematocrit (HCT), and below 15% for Reticulocyte percentage (RET%) to confirm the appropriate precision of the instrument.

4. External Quality Assessment Scheme

The Laboratories (or as otherwise approved by *WADA*) shall participate in and meet the requirements of *WADA's* EQAS for blood variables. The external quality controls shall be analyzed multiple times consecutively (based on the EQAS rules), and then the mean results of the following blood variables (full blood count) shall be returned:

Red Blood Cell (Erythrocyte) Count	RBC
Mean Corpuscular Volume	MCV
Haematocrit	HCT
Haemoglobin	HGB
Mean Corpuscular Haemoglobin	MCH
Mean Corpuscular Haemoglobin Concentration	MCHC
White Blood Cell (Leukocyte) Count	WBC
Platelet (Thrombocyte) Count	PLT
Reticulocytes Percentage	RET%

Laboratories or *WADA*-Approved Laboratory for the *ABP* may also participate in ring tests between laboratories (hospitals, clinics, etc.) using the same technology and the same procedure.

5. Analysis of Blood *Sample*

The temperature data logger shall be stopped before *Sample* homogenization[2]. The blood *Sample* shall be homogenized for a minimum period of 15 minutes using an appropriate mixer (e.g. roller mixer) prior to analysis.

The blood *Sample* shall be analyzed twice consecutively.

Absolute differences between the two consecutive analyses shall be equal or less than each of the following criteria in order to accept the results:

- 0.1g/dL for HGB analysis;

[2] In case the temperature data logger accompanies multiple *Samples*, and that these *Samples* are analyzed in the same batch by the Laboratory, the temperature data logger shall be stopped before the homogenization of the first *Sample*. The Laboratory shall proceed with the analysis of all *Samples* associated to the temperature data logger without delay.

- 0.15 absolute difference for RET% analysis if either the first or second measurement is lower or equal to 1.00%; otherwise 0.25 absolute difference.

The data from the second injection is used to confirm the first injection data. Therefore, if the absolute differences between the results of the analyses are within the criteria above, then only the first injection data is reported into *ADAMS*. If the absolute differences between the results of the two analyses are greater than those defined above, the analysis shall be started again in accordance with section 5 above.

The requirements for an Initial *Testing* Procedure, an "A" *Sample* Confirmation Procedure and a "B" *Sample* Confirmation Procedure, as defined in the ISL, shall not be applicable to blood *Samples* analyzed for the purposes of the *ABP*.

6. Reporting

The Laboratory or *WADA*-Approved Laboratory for the *ABP* shall promptly report into ADAMS the raw temperature profile recorded by the temperature data logger. The filename shall consist in the concatenation of the data logger ID with the date of *Sample* reception by the lab ("YYYY-MM-DD" in local time) separated by an underscore. For example, for a data logger ID "KG34V10" and a date of sample reception "2015-03-25", the Laboratory or *WADA*-Approved Laboratory for the *ABP* shall report the temperature profile under the filename "KG34V10_2015-03-25.txt". The Laboratory or *WADA*-Approved Laboratory for the *ABP* shall report the temperature profile before the test results of the *Sample*.

The Laboratory or *WADA*-Approved Laboratory for the *ABP* shall then report the following into *ADAMS*:

- *Sample* code;
- Type of test (*Out of Competition*/*In-Competition*);
- Sport and discipline;
- Date and time of receipt of the *Sample*;
- Date and time of analysis of the *Sample*;
- The name of the *Testing* Authority;
- The name of the Sample Collection Authority;
- Type of *Sample* (blood Passport);
- Type of analyzer;
- Test results (other variables may be included for quality purposes):

Blood Variable		Unit(s)
Haemoglobin	HGB	g/dL
Hematocrit	HCT	%
Immature Reticulocyte Fraction	IRF	%
Mean Corpuscular Haemoglobin	MCH	pg
Mean Corpuscular Haemoglobin Concentration	MCHC	g/dL
Mean Corpuscular Volume	MCV	fL

OFF-Score	-	-
Platelets	PLT	10^3/uL
Red Blood Cell Distribution Width	RDW-SD	fL
Red Blood Cells	RBC	10^6/uL
Reticulocytes – in absolute number	RET	10^6/uL
Reticulocytes Percentage	RET%	%
White Blood Cells	WBC	10^3/uL

3.3 Endogenous Anabolic Androgenic Steroids Measurement and Reporting

WADA Technical Document – TD2018EAAS

Document Number:	TD2018EAAS	Version Number:	1.0
Written by:	*WADA* Laboratory Expert Group	Approved by:	*WADA* Executive Committee
Date:	16 May 2018	Effective Date:	1 September 2018

1.0 Introduction

The purpose of this Technical Document (TD) is to harmonize the approaches to the measurement and reporting of Endogenous Anabolic Androgenic Steroids (EAAS) in urine *Samples*, including data in support of the steroidal module of the *Athlete Biological Passport* (*ABP*) (the steroidal Passport).

EAAS concentrations and their ratios form the urinary "steroid profile", which may be altered following the administration of synthetic forms of EAAS, in particular testosterone (T), its precursors [for example androstenediol, androstenedione and prasterone (dehydroepiandrosterone or DHEA)], or its active metabolite [dihydrotestosterone (DHT)], as well as epitestosterone (E).

The steroidal module of the *ABP* utilizes the Adaptive Model to identify an *Atypical Passport Finding* (*ATPF*), which triggers the performance of Confirmation Procedures. It is also useful for intelligent longitudinal *Target Testing* of an *Athlete*. Furthermore, an abnormal "steroid profile" (obtained from a single urine *Sample*) or an atypical steroidal Passport (including "steroid profiles" obtained from a series of *Samples* collected over a period of time), may be used as a means to pursue an anti-doping rule violation (ADRV).

EAAS Analytical Testing and reporting follows a two-step procedure. An Initial Testing Procedure is conducted to estimate the "steroid profile" of the *Athlete's Sample*. A subsequent Confirmation Procedure is performed when the estimated "steroid profile" constitutes an *ATPF*, as determined by the Adaptive Model, or represents a "suspicious steroid profile" (SSP) finding, or upon request from the Athlete Passport Management Unit (APMU), the Testing Authority or *WADA*.

The Confirmation Procedure includes the quantification of the *Markers* of the "steroid profile" as described in this TD as well as Gas Chromatography – Combustion - Isotope Ratio Mass Spectrometry (GC/C/IRMS) analysis, which is considered in a separate TD (TD IRMS) [1].

1.1 The “Steroid Profile”

Each urine *Sample* shall be analyzed to determine its “steroid profile”.

For the purposes of this TD, the “steroid profile” is composed of the following *Markers* (as free steroid content obtained from the free steroid fraction plus those released from the conjugated fraction after hydrolysis with β-glucuronidase from *E. coli*):

- Androsterone (A)
- Etiocholanolone (Etio)
- 5α-Androstane-3α,17β-diol (5αAdiol)
- 5β-Androstane-3α,17β-diol (5βAdiol)
- Testosterone (T)
- Epitestosterone (E).

and the following ratios:

- T/E
- A/T
- A/Etio
- 5αAdiol/5βAdiol
- 5αAdiol/E.

The administration of EAAS can alter one or more of the *Markers* and/or ratios of the urinary “steroid profile”, resulting in increase or decrease of concentrations and/or ratios of specific pairs of steroid *Metabolites* [2-4].

Additionally, alteration of the urinary “steroid profile” can occur for a number of reasons including, but not limited to, the following confounding factors:

- the administration of other anabolic steroids (*e.g.* stanozolol);
- the administration of human chorionic gonadotrophin (hCG) in males;
- the administration of aromatase inhibitors and anti-estrogens;
- the administration of inhibitors of 5α-reductase (*e.g.* finasteride);
- intake of alcohol (ethanol);
- the administration of ketoconazole or other similar compounds;
- the use of masking agents (*e.g.* probenecid) and diuretics; or
- microbial growth.

2.0 Initial Testing Procedure

The Laboratory shall use a validated Initial Testing Procedure that is Fit-for-Purpose to estimate the *Markers* of the urinary "steroid profile" in the range of values determined in males and females.

The Initial Testing Procedure is conducted on a single Aliquot.

2.1 Method Characteristics

- Gas chromatography combined with mass spectrometry (GC-MS or GC-MS/MS) of TMS derivatives (keto- and hydroxyl- groups) is required;
- Calibration standard(s) or a calibration curve should be included in each sequence of analysis;
- At least two urine quality control (QC) samples containing varying and representative concentrations of the *Markers* of the "steroid profile" should be included in each sequence of analysis;
- The enzymatic hydrolysis shall be carried out with purified β-glucuronidase from *E. coli* (*H. pomatia* mixtures are not acceptable);
- The completeness of hydrolysis of the glucuroconjugated urinary steroids shall be controlled with isotopically labeled A-glucuronide (or an equivalent scientifically recognized alternative);
- The completeness of the derivatization shall be controlled through the monitoring of mono-O-TMS vs. di-O-TMS derivative of A;
- When needed, the volume[1] of the *Sample* Aliquot may be adjusted as a function of its specific gravity (SG) and of the sex of the *Athlete*;
- The T/E ratios shall be determined from the ratios of the corrected chromatographic peak areas or peak heights[2];

[1] Much smaller concentrations of T and E are generally present in *Samples* from females and in those *Samples* with low SG; therefore, larger Aliquot volumes may be required for a reliable measurement.

[2] Ratios of T and E peak heights or peak areas corrected against a calibrator or a calibration curve (same mass or same ion transition screened for both steroids).

- The linearity of the method, established during method validation, shall cover the ranges of *Marker* concentrations normally found in males and females - the limit of quantification (LOQ) for T and E shall not be greater than 2 ng/mL[3];
- The relative standard combined Measurement Uncertainty [u_c (%)] for the determination of A, Etio, 5αAdiol, 5βAdiol, T and E, as estimated during method validation of the Initial Testing Procedure, shall be:
  - Not greater than 30% at the respective LOQ;
  - Not greater than 20% (for A and Etio) or 25% (for the Adiols) at five (5) times the LOQ;
  - Not greater than 20% (for T and E) when the concentration is greater than 5 ng/mL.
- The u_c (%) for determinations of T/E ratios calculated from the corrected chromatographic peak areas or heights shall be:
  - Not greater than 15% when the concentrations of T and E are both greater (>) than 5 ng/mL;
  - Not greater than 30% when the concentrations of T and/or E are equal to or lower (≤) than 5 ng/mL.
- Evidence of microbial degradation [*e.g.* presence of indicators of 3α-hydroxysteroid dehydrogenase (HSD) activity] and the presence of 5α-reductase inhibitors (*e.g.* finasteride), ethanol *Metabolite(s)* and ketoconazole (and similar substances) shall be monitored by the Laboratory[4].

[3] The LOQ for the "steroid profile" *Markers* shall be determined as the lowest concentration that can be measured within a u_c (%) of 30%.

The LOQ determined from the method validation of T, E, A, Etio, 5αAdiol and 5βAdiol shall be recorded in *ADAMS* by the Laboratory. The LOQ values shall be updated in *ADAMS* whenever a significant change is made to the analytical method.

[4] The direct enzymatic hydrolysis of urine *Samples* may increase the effects of microbial contamination.

2.2. Reporting the "steroid profile" from the Initial Testing Procedure

Following the performance of the Initial Testing Procedure, the Laboratory shall report in *ADAMS* the "steroid profile" for each *Sample* analyzed[5, 6], including:

- the SG[7] of the *Sample*;
- the concentrations of T, E, A, Etio, 5αAdiol and 5βAdiol[8, 9, 10];

[5] This also applies when more than one (1) *Sample* from the same *Athlete*, which are linked to a single Sample Collection Session, are analyzed.

[6] The Laboratory shall report in *ADAMS* the *Sample*'s "steroid profile", as determined during the Initial Testing Procedure, in cases when no *Prohibited Substance* or *Prohibited Method* is detected in the *Sample* [while reporting the test result as a Negative Finding], as well as in cases when the Laboratory confirms the presence of a *Prohibited Substance* or *Prohibited Method* [while reporting the result as an *Adverse Analytical Finding (AAF*) or *Atypical Finding (ATF)*, as applicable, for the *Prohibited Substance* or *Prohibited Method* detected].

[7] As determined by the Laboratory using, for example, a refractometer.

[8] When reporting the "steroid profile" in *ADAMS*, the Laboratory shall report the values of concentrations for T, E, A, Etio, 5αAdiol and 5βAdiol, and the T/E ratio (**without adjustment for the urine SG or correction to a specific number of significant figures**). An automatic correction of reported values to 2 significant figures will be made in *ADAMS* upon application of the Adaptive Model of the *ABP*.

[9] When the Initial Testing Procedure measurement of a "steroid profile" *Marker* is not possible due to, for example, dilution, unusual matrix interferences, inhibition of the enzymatic hydrolysis or incomplete derivatization, the Laboratory should repeat the analysis with an alternative, validated *Sample* preparation procedure (*e.g.* concentrating the *Sample* or taking larger Aliquot volumes, application of solid phase extraction, extraction with a different solvent or other equivalent procedure). If, however, the *Marker* of the "steroid profile" cannot be quantified, the concentration of the *Marker* shall be reported as "-1". When the chromatographic peak signal for a *Marker* cannot be detected (*i.e.* is below the detection capability of the assay), the concentration of the *Marker* shall be reported as "-2" (see Table 1).

[10] The Laboratory may also provide information on other steroidal parameters such as dehydroepiandrosterone (DHEA) and 6α-hydroxy-androstenedione at the request of the Testing Authority, Results Management Authority or the APMU.

- the T/E ratio[2, 11];
- signs of microbial activity in the *Sample*, *e.g.* ratios of 5α-androstanedione (5αAND) to A and 5β-androstanedione (5βAND) to Etio[12];
- the presence or absence in the *Sample* of substance(s) that may alter the "steroid profile" [12].

In cases when a *Sample* is not consistent with human urine (*e.g.* SG ≤ 1.001, creatinine ≤ 5 mg/dL [5], non-physiological salt concentration, abnormal pH values, absence or abnormally low levels of endogenous steroids, corticosteroids, proteins), the Laboratory shall:

- report the finding as an *AAF* for *Tampering* or *Attempted Tampering* (class M2.1 of the *Prohibited List*) if the Laboratory can unequivocally identify the nature of the liquid (*e.g.* water, liquor, synthetic urine) provided as the adulterated *Sample;* or
- report the finding as an *AAF* for *Tampering* or *Attempted Tampering* if the Laboratory has reason to believe that the *Sample* could have been altered in any manner, improperly interfered with, or potentially been the subject of any fraudulent conduct that could alter the results of Analytical Testing; or
- inform the Testing Authority about the suspicious finding and request further information which may support the reporting of this finding as an *AAF* for *Tampering* or *Attempted Tampering* (e.g. longitudinal "steroid profile" data for the *Athlete*); or
- report the finding as an *ATF* for *Tampering* or *Attempted Tampering* and include a comment in *ADAMS* advising the Testing Authority to perform further investigations (*e.g.* additional analyses on the *Sample*, *Target Testing* the *Athlete*) in order to establish whether *Tampering* of the *Sample* has occurred and the finding be treated as an Anti-Doping Rule Violation.

[11] The values of A/T, A/Etio, 5αAdiol/5βAdiol and 5αAdiol/E ratios are automatically computed in *ADAMS* after the reporting of the "steroid profile" by the Laboratory.

[12] A *Sample* showing signs of microbial degradation or containing any of the substances that may cause an alteration of the "steroid profile" (see section 1.1) may not be suitable for inclusion in the "longitudinal steroid profile". These findings are to be considered by the APMU during the results management process when evaluating the analytical data for the *Sample* and assessing the possible pathological or confounding conditions that may have impacted the *Sample's* "steroid profile".

2.2.1 Validity of (the "steroid profile" of) the *Sample*

The validity of the *Sample* will be determined automatically upon reporting the "steroid profile" in *ADAMS* in accordance to:

a) **"Invalid"**: **only when the *Sample* shows signs of extensive degradation**[13], as determined by:

- 5αAND/A ≥ 0.1, and/or
- 5βAND/Etio ≥ 0.1

b) "**Valid"**: **in all other situations**, including:

- LOD ≤ [T and/or E] < LOQ

  When the concentration of either T and/or E in the *Sample* Aliquot analyzed cannot be quantified, but its chromatographic peak signal is still detectable (e.*g.* S/N > 3) and the T/E ratio can be determined from the corrected chromatographic peak areas or peak heights[2], the calculated value of the T/E ratio shall be reported in *ADAMS*, whereas the concentration of T and/or E, as applicable, shall be reported as "-1" (Table 1)[9].

- [T] < LOD

  If the chromatographic peak signal for T cannot be detected, the concentration of T shall be reported as "-2" and the T/E value shall be reported as "-1" (Table 1)[9] and:

  i. for [E] ≥ LOQ, a comment shall be included in *ADAMS* stating that the T/E ratio could not be measured because the concentration of T was below the detection capability of the assay; or

  ii. for LOD ≤ [E] < LOQ, the concentration of E shall be reported as "-1" [9] and a comment shall be included in *ADAMS* stating that the T/E ratio could not be measured because the concentrations of T and E could not be measured.

[13] In addition, following the reporting of the "steroid profile" in *ADAMS* by the Laboratory, the *Sample* may be evaluated as "invalid" by the APMU upon review of the "steroid profile" data, for example, by considering the presence of substances that may alter the "steroid profile" in the *Sample*.

- [E] < LOD

  If the chromatographic peak signal for E cannot be detected, the concentration of E shall be reported as "-2" [9] (Table 1) and:

  i. for [T] ≥ LOQ, the T/E ratio shall be calculated on the basis of the Laboratory's LOD value for E (*e.g.* if T concentration is 3 ng/mL and E cannot be detected, and the Laboratory's LOD for E is 0.5 ng/mL, the T/E shall be reported as 6.0) (Table 1). A comment shall be included in *ADAMS* stating that the T/E ratio could not be measured accurately because the concentration of E was below the detection capability of the assay; or

  ii. for LOD ≤ [T] < LOQ, the T/E ratio and the concentration of T shall be reported as "-1" [9] and a comment shall be included in *ADAMS* stating that the T/E ratio could not be measured accurately because the concentrations of T and E could not be measured (Table 1).

- Both [T and E] < LOD:

  If the chromatographic peak signals for both T and E cannot be detected, the concentrations of T and E shall be reported as "-2" and the T/E value shall be reported as "-2" (Table 1)[9]. A comment shall be included in *ADAMS* stating that the T/E ratio could not be measured because the concentrations of both T and E were below the detection capability of the assay.

- When other *Marker*(s) of the "steroid profile" cannot be measured accurately:

  o LOD ≤ [*Marker*] < LOQ

  If the concentration of the *Marker* in the Aliquot is below the LOQ of the assay, but its chromatographic peak signal is still detectable (*i.e.* above the LOD of the assay), the concentration of the *Marker* shall be reported as "-1" [9].

  o [*Marker*] < LOD

  If the chromatographic peak signal for the *Marker* cannot be detected (*i.e.* below the LOD of the assay), the concentration shall be reported as "-2" [9].

- When less extensive microbial contamination is detected which shall be reported in *ADAMS*[12] as:

  5αAND/A ratio and/or 5βAND/Etio ratio between 0.05 and 0.1.

- When the Laboratory reports an *AAF* or an *ATF* for a *Prohibited Substance* that may alter the "steroid profile" (*e.g.* an anabolic steroid, hCG in males, a diuretic or masking agent)[12];
- When the Laboratory detects and reports the presence in the *Sample* of other substances that may cause an alteration of the "steroid profile" (see section 1.1)[12, 14].

[14] It is mandatory that the Laboratory tests at least for the presence of conjugated *Metabolite(s)* of ethanol [*e.g.* ethanol glucuronide (EtG)], inhibitors of 5α-reductase and ketoconazole during the Initial Testing Procedure and report the estimated concentration of EtG if above 5 μg/mL (without the need to report the Measurement Uncertainty).

Table 1. Summary of conditions for reporting T and E concentrations and T/E ratio.

Concentration of T	Concentration of E	T/E ratio
Chromatographic peak signal of T measured at or above the LOQ. $[T] \geq LOQ_{(T)}$ **Report T as measured**	Chromatographic peak signal of E measured at or above LOQ. $[E] \geq LOQ_{(E)}$ **Report E as measured**.	**Report T/E as determined** from corrected peak heights/areas
	Chromatographic peak signal of E detected, but below LOQ. $LOD_{(E)} \leq [E] < LOQ_{(E)}$ **Report E as "-1"** [9]	
	Chromatographic peak signal of E not detected. $[E] < LOD_{(E)}$ **Report E as "-2"** [9]	**Report T/E as T/LOD$_{(E)}$** *Comment in ADAMS*: T/E ratio could not be measured accurately because the concentration of E was below the detection capability of the assay
Chromatographic peak signal of T detected, but below the LOQ. $LOD_{(T)} \leq [T] < LOQ_{(T)}$ **Report T as "-1"** [9]	Chromatographic peak signal of E measured at or above LOQ. $[E] \geq LOQ_{(E)}$ **Report E as measured**	**Report T/E as measured** from corrected peak heights/areas
	Chromatographic peak signal of E detected, but below LOQ. $LOD_{(E)} \leq [E] < LOQ_{(E)}$ **Report E as "-1"** [9]	
	Chromatographic peak signal of E not detected. $[E] < LOD_{(E)}$ **Report E as "-2"** [9]	**Report T/E as "-1"** *Comment in ADAMS*: T/E ratio could not be measured accurately because the concentrations of T and E could not be measured
Chromatographic peak signal of T not detected. $[T] < LOD_{(T)}$ **Report T as "-2"** [9]	Chromatographic peak signal of E measured at or above LOQ. $[E] \geq LOQ_{(E)}$ **Report E as measured**	**Report T/E as "-1"** *Comment in ADAMS*: T/E ratio could not be measured because the concentration of T was below the detection capability of the assay
	Chromatographic peak signal of E detected but below LOQ. $LOD_{(E)} \leq [E] < LOQ_{(E)}$ **Report E as "-1"** [9]	**Report T/E as "-1"** *Comment in ADAMS*: T/E ratio could not be measured because the concentrations of T and E could not be measured
	Chromatographic peak signal of E not detected. $[E] < LOD_{(E)}$ **Report E as "-2"** [9]	**Report T/E as "-2"** *Comment in ADAMS*: T/E ratio could not be measured because the concentrations of both T and E were below the detection capability of the assay

3.0 Confirmation Procedures

Confirmation Procedures for the exogenous administration of EAAS include the GC-MS or GC-MS/MS quantification[15] and GC/C/IRMS analysis of the *Marker(s)* of the "steroid profile".

In addition, the Laboratory shall confirm the presence or absence, as applicable, of the confounding factors of the "steroid profile" as described in section 1.1, *i.e.* conjugated *Metabolite(s)* of ethanol (*e.g.* EtG), inhibitors of 5α-reductase (*e.g.* finasteride), ketoconazole as well as the signs of microbial degradation including, for example, the presence of the free forms of T, 5αAND or 5βAND.

3.1 "*Atypical Passport Finding* Confirmation Procedure Request (*ATPF*-CPR)"

Following the Laboratory's reporting of a *Sample*'s "steroid profile" in *ADAMS*, the *Sample* record is matched with a Doping Control Form (DCF), which allows the inclusion of the *Sample*'s "steroid profile" in the *Athlete's* steroidal Passport in *ADAMS*.

The Adaptive Model will generate an "*ATPF*-CPR" notification when the *Sample's* T/E ratio is abnormally high, as determined by the Adaptive Model, when compared with the previous longitudinal T/E values of the *Athlete*.

The Laboratory shall proceed with the Confirmation Procedures when receiving an "*ATPF*-CPR" notification for the *Sample*, except in the following cases:

- If the APMU advises the Laboratory, in writing, not to confirm the "steroid profile" of the *Sample* based on justifiable reason(s). Justification for not proceeding with a Confirmation Procedure for an *ATPF* may include:
    - the presence of EtG in a *Sample* from an *Athlete* with previous similar findings in his/her Passport with negative GC/C/IRMS results (indicating a pattern of alcohol abuse); or
    - if other *AAFs* have been reported for the *Sample*, which would likely lead to a maximum sanction.

[15] For T/E values, only T needs to be confirmed if the concentration levels of E or the volume of the *Sample* is not sufficient.

In such cases, the Laboratory shall update the *ADAMS* report for the *Sample* with a comment stating that the APMU requested not to perform the Confirmation Procedure(s). The APMU shall also update the APMU Report in *ADAMS* with an explanation of why the Confirmation Procedure(s) were not necessary.

- In addition, the GC/C/IRMS Confirmation Procedure for an *ATPF* is not mandatory if the GC-MS or GC-MS/MS quantitative analysis does not confirm the abnormally high T/E ratio of the *Sample* (see section 3.5 below). In such cases, the Laboratory shall report the confirmed values of the *Markers* of the "steroid profile" in *ADAMS* (see section 3.6 below) with a comment stating that the GC/C/IRMS analysis was not performed because the abnormally high T/E ratio was not confirmed.

The Adaptive Model will also determine abnormal values of the other ratios of the "steroid profile" (A/T, A/Etio, 5αAdiol/5βAdiol, 5αAdiol/E). However, in such cases the Laboratory will not receive an automatic "*ATPF*-CPR" notification through *ADAMS*. Instead, the Athlete Passport Management Unit (APMU) will advise the Testing Authority on whether the *Sample* shall be subjected to Confirmation Procedures. Therefore, in these cases the Laboratory shall receive a request from the Testing Authority before proceeding with the Confirmation Procedure(s)[16].

3.2 "Suspicious Steroid Profile Confirmation Procedure Request (SSP-CPR)"

The Laboratory will receive a "SSP-CPR" notification through *ADAMS* if:

1) The *Sample* is matched with a DCF in *ADAMS*, but there is no existing steroidal Passport of the *Athlete* in *ADAMS* (*i.e.* this is the first *Sample* in the *Athlete's* steroidal Passport), or

   The *Sample* cannot be matched with a DCF in *ADAMS* within fourteen (14) calendar days after the reception date of the *Sample* by the Laboratory, and therefore the "steroid profile" of the *Sample* cannot be processed by the Adaptive Model in *ADAMS*,

   and

[16] Unless covered by an agreement between the Laboratory and the Testing Authority.

2) The *Sample's* "steroid profile" meets **any** of the following criteria:

- o T/E ratio (calculated from the corrected chromatographic peak areas or heights) greater than 4.0;
- o A/T ratio less than 20;
- o 5αAdiol/5βAdiol ratio greater than 2.4;
- o concentration of T or E (adjusted for the SG[7, 17]) greater than 200 ng/mL in males or greater than 50 ng/mL in females;
- o concentration of A or Etio (adjusted for the SG[7, 17]) greater than 10,000 ng/mL;
- o concentration of 5αAdiol (adjusted for the SG[7, 17]) greater than 250 ng/mL in males or greater than 150 ng/mL in females, combined with a 5αAdiol/E ratio greater than 10 in either sex.

- Upon receipt of the "SSP-CPR" notification, the Laboratory shall proceed with the Confirmation Procedure(s) unless, after contacting the Testing Authority, the Testing Authority can justify in writing within seven (7) calendar days that the Confirmation Procedure(s) is not necessary. Justification for not proceeding with the Confirmation Procedure may include, for example, a naturally elevated T/E ratio confirmed by previous Analytical Testing, or a T/E ratio between 4.0 and 6.0 for the first test on the *Athlete*, or if other *AAF*s have been reported for the *Sample*, which would likely lead to a maximum sanction;
- If the Testing Authority justifies that confirmation is not necessary, the Laboratory shall update the *ADAMS* report for the *Sample* with a comment stating that the Testing Authority considered that the Confirmation Procedure(s) was not necessary and detail the explanation provided by the Testing Authority. If the Testing Authority does not justify that confirmation is not necessary, the Laboratory shall proceed with the confirmation analyses.

[17] The concentrations are adjusted to a urine SG[7] of 1.020 based on the following equation (free and hydrolyzed glucuroconjugated steroids).

$$\mathbf{Conc_{corr} = Conc_{measured} * (1.020 - 1) / (SG - 1)}$$

In cases when the Laboratory receives "*ATPF*-CPR" or "SSP-CPR" for two (2) or more *Samples*, which are linked to a single *Sample* collection session from the same *Athlete*, the Laboratory, in consultation with the Testing Authority, shall prioritize the confirmation of the *Sample* with the highest concentration levels of the *Markers* of the "steroid profile".

When the Laboratory receives an "*ATPF*-CPR" or a "SSP-CPR" for a *Sample* for which *AAF(s)* have been reported for other *Prohibited Substance(s)* or *Method(s)*, the Laboratory should consult the Testing Authority about the need to conduct the Confirmation Procedures for the *Markers* of the "steroid profile".

3.3 Confirmation Procedure Requests from the APMU, the Testing Authority or *WADA*.

Confirmation Procedures for the "steroid profile" may be also performed on *Samples* at the request of the APMU, the Testing Authority or *WADA*.

In addition, a Laboratory may have a contractual agreement in place with the Testing Authority to conduct the Confirmation Procedures when a *Sample* meets any of the analytical criteria of a "suspicious steroid profile" or at the Laboratory's discretion based on its expertise. In such circumstances, the Laboratory may proceed to the confirmation of the "suspicious steroid profile" immediately without waiting for an "*ATPF*-CPR" or a "SSP-CPR" through *ADAMS.*

3.4 GC-MS or GC-MS/MS quantification Confirmation Procedure

The Laboratory shall identify (in compliance with the TD IDCR [6]) and quantify all the *Markers* of the "steroid profile" in one additional *Sample* Aliquot by a validated Fit-for-Purpose GC-MS or GC-MS/MS quantification method.

The Laboratory shall confirm quantitatively all the *Markers* of the "steroid profile" before proceeding with the GC/C/IRMS analysis.

3.4.1 Method Characteristics for the GC-MS or GC-MS/MS quantification Confirmation Procedure

The same analytical requirements presented in section 2.1 shall apply, with the following modifications:

- A Solid Phase Extraction (SPE) shall be performed prior to the enzymatic hydrolysis of the *Sample*;
- Calibration standards and urine QC samples containing representative levels of the *Markers* of the "steroid profile" shall be included;
- The u_c (%) shall be not greater than 15% for determinations of A, Etio, 5αAdiol and 5βAdiol at concentrations representing five times the respective LOQ;

- For determinations of T, E and T/E ratios, the u_c (%) shall be not greater than 15% when the concentrations of T and E are greater than 5 ng/mL.

3.5 GC/C/IRMS Confirmation Procedure

Technical and reporting requirements for the GC/C/IRMS Confirmation Procedure are specified in the TD IRMS [1].

- In the case of an *ATPF*-CPR, GC/C/IRMS analysis is not mandatory when the confirmed T/E value is below the confirmation T/E threshold calculated by the Adaptive Model and provided within the *ATPF*-CPR notification received from *ADAMS;*
- For other Confirmation Procedure requests (*i.e.* SSP-CPR or upon APMU/Testing Authority/*WADA* request), when the quantitative GC-MS or GC-MS/MS Confirmation Procedure does not confirm the values reported from the Initial Testing Procedure (taking into consideration the expanded uncertainty of the measurement), the Laboratory shall consult the Testing Authority to determine if the GC/C/IRMS analysis is necessary. In such cases, the Testing Authority shall consult with the APMU of the Passport Custodian in order to assess whether the GC/C/IRMS analysis is still necessary. In the event that GC/C/IRMS analysis is deemed unnecessary, the Laboratory shall update the *ADAMS* report for the *Sample* with the newly confirmed values of the “steroid profile” and include a comment that GC/C/IRMS analysis was not necessary. The APMU shall also update the APMU Report in *ADAMS* with an explanation of why the GC/C/IRMS Confirmation Procedure was not necessary.

3.6 Reporting Results from the Confirmation Procedures

Following the performance of the Confirmation Procedure(s) on the "A" or the "B" *Sample*[18], the Laboratory shall report in *ADAMS*:

- the SG[7] of the *Sample* (determined from a new Aliquot of the "A" or "B" *Sample*, as applicable)*;*
- the confirmed values (*e.g.* concentrations, T/E ratio) of the *Markers* of the "steroid profile", without adjustment for the SG of the *Sample* [8, 9, 11];
- the associated u_c expressed in units;
- the GC/C/IRMS confirmation results, if determined (see section 3.5 and TD IRMS [1]);
- the confirmed results for signs of microbial contamination (*e.g.* 5αAND/A, 5βAND/Etio, T_{free} / T_{total} [19]);
- the confirmed presence or absence of conjugated *Metabolite(s)* of ethanol, inhibitors of 5α-reductase (*e.g.* finasteride), ketoconazole or any other substances that might have altered the "steroid profile", if applicable. The Laboratory shall report the confirmed estimated levels of EtG if above 5 μg/mL (without the need to report the Measurement Uncertainty for this determination).

Following the confirmation of the "steroid profile", the Laboratory shall update the *ADAMS* test result record for the *Sample* (as *AAF*, *ATF*, or "Negative") based on the results of the GC/C/IRMS Confirmation Procedure, if performed, in accordance with the TD IRMS [1]).

[18] When an *AAF* is reported for the *Marker(s)* of the "steroid profile" based on the results of a GC/C/IRMS analysis performed on the "A" *Sample*, only the GC/C/IRMS analysis shall be repeated during the "B" *Sample* Confirmation Procedure, if applicable. Refer to the TD IRMS [1].

[19] In addition to the determination of the 5αAND/A and 5βAND/Etio ratios as signs of microbial contamination, as described in section 2.2.1 for the Initial Testing Procedure, the determination during the Confirmation Procedure of an elevated ratio of free Testosterone to total Testosterone (T_{free} / T_{total} > 0.05) will also invalidate (the "steroid profile" of) the *Sample*.

3.7 Additional Analyses: Steroid Ester(s) and DNA

When matched blood *Samples* have been collected during the same Sample Collection Session as urine *Samples* identified with an atypical or suspicious "steroid profile", Laboratories, in consultation with the Testing Authority, should consider conducting analysis to detect the presence of steroid ester(s) in the associated serum/plasma.

It is recommended that confirmation analyses for steroid ester(s) in serum/plasma be conducted prior to the performance of the GC/C/IRMS analysis in urine. The detection of steroid ester(s) in serum/plasma also constitutes an unequivocal demonstration of the exogenous origin of the steroid(s). On the other hand, the absence of detectable steroid ester(s) in serum/plasma shall not invalidate an *AAF* based on the GC/C/IRMS analysis in urine.

The performance of a DNA analysis may also be considered to establish, in conjunction with the *Athlete's* "longitudinal steroid profile", the origin of the *Sample*(s).

4.0 References

1. *WADA* Technical Document TD IRMS (current version): Detection of synthetic forms of Endogenous Anabolic Androgenic Steroids by GC/C/IRMS.

https://www.wada-ama.org/en/resources/search?f[0]=field_resource_collections%3A30

2. Mareck U, Geyer H, Opfermann G, Thevis M, Schänzer W. Factors influencing the steroid profile in doping control analysis. *J Mass Spectrom*. **43**(7):877-91, 2008.

3. Ayotte C. Detecting the administration of endogenous anabolic androgenic steroids. *Handb Exp Pharmacol.* **195**:77-98, 2010.

4. Kuuranne T, Saugy M, Baume N. Confounding factors and genetic polymorphism in the evaluation of individual steroid profiling. *Br J Sports Med*. **48**(10):848-55, 2014.

5. J D Cook, Caplan YH, LoDico CP and Bush DM. The Characterization of Human Urine for Specimen Validity Determination in Workplace Drug Testing: A Review. *J Anal Toxicol* **24**: 579-588, 2000

6. *WADA* Technical Document TDIDCR (current version): Minimum Criteria for Chromatographic-Mass Spectrometric Confirmation of the Identity of Analytes for Doping Control Purposes.

https://www.wada-ama.org/en/resources/search?f[0]=field_resource_collections%3A30

3.4 Results Management Requirements and Procedures for the *Athlete Biological Passport* (ISTI Annex L)

L.1 Administrative Management

The *Anti-Doping Organization* (*ADO*) referred to throughout this Annex on Results Management is the *Passport* Custodian. As a rule, all requirements and procedures described in this Annex apply to all modules of the *Athlete Biological Passport* (*ABP)* except where expressly stated, or implied by the context.

These processes shall be administered and managed by an *Athlete Passport* Management Unit (APMU) on behalf of, or within, the *ADO*. The APMU will initially review profiles to facilitate targeting recommendations for the *ADO* when appropriate, or refer to the Experts as required. Management and communication of the biological data, APMU reporting and Expert reviews shall be recorded in *ADAMS* and be shared by the *Passport* Custodian with other *ADO(s)* with *Testing* jurisdiction over the *Athlete* to coordinate further Passport *Testing* as appropriate. A key element for *ABP* management and communication is the APMU Report in *ADAMS* which provides an overview of the current status of the *Athlete*'s Passport including the latest targeting recommendations and a summary of the Expert reviews.

This Annex describes a step-by-step approach to the review of an *Athlete's* Passport:

a) The review begins with the application of the Adaptive Model.
b) In case of an *Atypical Passport Finding* (*ATPF*) or when the APMU considers that a review is otherwise justified, an Expert conducts an initial review and returns an evaluation based on the information available at that time.
c) In case of a "Likely doping" initial review, the Passport is then subjected to a review by three Experts including the Expert who conducted the initial review.
d) In case of a "Likely doping" consensus of the three Experts, the process continues with the creation of an *ABP* Documentation Package.
e) An *Adverse Passport Finding (APF)* is reported by the APMU to the *ADO* if the Experts opinion is maintained after review of all information available at that stage, including the *ABP* Documentation Package.
f) The *Athlete* is notified of the *Adverse Passport Finding (APF)* and offered the opportunity to provide explanations.
g) If after review of the explanations provided by the *Athlete*, the Experts maintain their unanimous conclusion that it is highly likely that the *Athlete* used a *Prohibited Substance* or a *Prohibited Method*, an anti-doping rule violation (ADRV) is asserted against the *Athlete* by the *ADO* and disciplinary proceedings are initiated (*Code* Article 7.5).

[Comment: The *ABP* follows a similar logical structure to Results Management for analytical *Testing*, with both processes culminating in a possible ADRV based on, respectively, *Code* Article 2.2 and *Code* Article 2.1. An *ATPF* is to the *ABP* what an *Atypical Finding (ATF)* is to analytical *Testing*; both require further investigation. Similarly, an *APF* is to the *ABP* what the *Adverse Analytical Finding (AAF)* is to analytical *Testing*; both require Results Management in accordance with *Code* Article 7.]

L.2 Initial Review Phase

L.2.1 Review by the Adaptive Model

The biological *Markers* of the *ABP* are automatically processed in *ADAMS* by the Adaptive Model. The Adaptive Model predicts for an individual an expected range within which a series of *Marker* values falls assuming a normal physiological condition. Outliers correspond to those values outside of the 99%-range, from a lower limit corresponding to the 0.5th percentile to an upper limit corresponding to the 99.5th percentile (1:100 chance or less that this result is due to normal physiological variation). A specificity of 99% is used to identify both haematological and steroidal *ATPFs*. In the case of sequence deviations (sequence *ATPFs*), the applied range is 99.9% (1:1000 chance or less that this is due to normal physiological variation).

An *ATPF* is a result generated by the Adaptive Model in *ADAMS* which identifies either a *Marker(s)* value(s) as being outside the *Athlete*'s intra-individual range or a longitudinal profile of *Marker* values (sequence deviations) as being outside expected ranges, assuming a normal physiological condition. An *ATPF* requires further attention and review.

The APMU may also submit a Passport to the Expert when there is no *ATPF* (see 2.2.3 below).

L.2.1.2 *ATPF* – Haematological Module

For the Haematological Module, an *ATPF* is generated when the haemoglobin concentration (HGB) and/or stimulation index OFF-score (OFFS) value of the last test falls outside the expected intra-individual ranges. Furthermore, the longitudinal profile composed of (up to) the last 20 valid HGB and/or OFFS values is also considered as an *ATPF* when deviating from the expected ranges, as determined by the Adaptive Model (sequence *ATPF*). An *ATPF* is only generated by the Adaptive Model based on values of the primary *Markers* HGB and OFFS or the sequence thereof.

L.2.1.3 *ATPF* – Steroidal Module

For the Steroidal Module, an *ATPF* is generated when at least one value of the ratios T/E, A/T, A/Etio, 5αAdiol/5βAdiol or 5αAdiol/E falls outside the expected intra-individual ranges. In addition, the "longitudinal steroid profile" composed of (up to)

the last 20 valid values of one of these five ratios is also considered as atypical when deviating from the expected ranges, as determined by the Adaptive Model (sequence *ATPF*).

In the case of a "longitudinal steroidal profile," an *ATPF* caused by an atypically high T/E value will trigger an *ATPF* Confirmation Procedure Request notification through *ADAMS* as established in the TDEAAS. When the Adaptive Model determines an *ATPF* for any of the other ratios of the "steroid profile" (A/T, A/Etio, 5αAdiol/5βAdiol, 5αAdiol/E), the APMU should advise the *Testing* Authority in the APMU Report, or via the *Passport* Custodian where appropriate, on whether the *Sample* should be subjected to a Confirmation Procedure.

Ratios coming from a *Sample* that showed signs of heavy microbial degradation, and ratios for which one or both of the concentrations were not measured accurately by the Laboratory as established in the TDEAAS, shall not be processed by the Adaptive Model. In the case where the Laboratory reports a factor that may otherwise cause an alteration in the steroid profile, such as the presence of ethanol glucuronide in the *Sample*, the APMU shall evaluate whether the steroid profile can still be processed by the Adaptive Model and the *Sample* be subjected to a Confirmation Procedure.

L.2.1.4 Departure from WADA ABP requirements

If there is a departure from WADA ABP requirements for Sample collection, transport and analysis, the biological result obtained from this Sample affected by the non-confirmity shall not be considered in the Adaptive Model calculations (for example, reticulocytes are affected but not haemoglobin).

The part of the result which is not affected by the non-conformity can still be considered in the Adaptive Model calculations. In such case, the APMU shall provide the specific explanations supporting the inclusion of the results. In all cases, the Sample shall remain recorded in the Athlete's Passport. The Experts may include all results in their review provided that their conclusions may be validly supported in the context of the non-conformity.

L.2.2 The Initial Expert Review

A Passport generating an *ATPF,* or for which a review is otherwise justified, shall be sent by the APMU to an Expert for anonymous review in *ADAMS*. This should take place no later than 7 working days following the generation of the *ATPF* in *ADAMS*. The review of the Passport shall be conducted anonymously (without reference to the specific *Athlete* by name) based on the profile and other basic information (e.g. competition schedules), which could be already available.

The Experts shall be external to the APMU and to the *ADO*, except in the case described in 2.2.2 for the Steroidal Module.

L.2.2.1 Review – Haematological Module

If the Haematological Module generates an *ATPF* or if such review is otherwise requested by the APMU, then the results/profile must be reviewed by an Expert designated by the APMU.

L.2.2.2 Review - Steroidal Module

If a result rendered by a Laboratory represents an *ATPF* caused by an atypically high T/E value, the *Sample* will undergo a Confirmation Procedure, including GC-C-IRMS analysis. If the result of the GC-C-IRMS Confirmation Procedure is negative or inconclusive then the APMU shall seek an Expert review. An APMU or Expert review is not required when the GC-C-IRMS Confirmation Procedure renders an *Adverse Analytical Finding* (*AAF*).

If the first and unique result in a Passport is identified as atypical by the Adaptive Model (with a negative or inconclusive IRMS result, if applicable), the APMU may recommend the collection of an additional *Sample* before initiating the initial Expert review.

If the result represents an *ATPF* for any of the ratios A/T, A/Etio, 5αAdiol/5βAdiol, 5αAdiol/E, the APMU should evaluate the Passports and provide an APMU report in *ADAMS*.

When the APMU is associated to a Laboratory, it can replace the first external Expert and provide a review through the APMU Report in *ADAMS*.

L.2.2.3 Review in the absence of an ATPF

For both Modules, a Passport may also be sent for Expert review in the absence of an *ATPF* where the Passport includes other elements otherwise justifying a review. These elements may include, without limitation:

a) Data not considered in the Adaptive Model
b) Any abnormal levels and/or variations of *Markers*
c) Signs of hemodilution in the haematological Passport
d) Steroid levels in urine below the corresponding limit of quantification (LOQ) of the assay
e) Intelligence in relation to the *Athlete* concerned.

An Expert review initiated in the above-mentioned situations may result in the same consequences as an Expert review triggered by an *ATPF*.

L.2.3 Consequences of the Initial Review

Depending on the outcome of the initial review, the APMU will take the following action:

Expert Evaluation	**APMU Action**
Normal: Likely physiological condition	Continue normal *Testing* pattern.
Passport suspicious: Further data is required.	Alert *ADO* to do Target *Testing* and provide recommendations.
Likely doping: Considering the information within the *Athlete's* Passport, it is likely that the Passport is the result the *Use* of a *Prohibited Substance* or *Prohibited Method* and it is highly unlikely that it may be the result of a normal physiological or pathological condition.	Send to a panel of three Experts, including the initial Expert, as per section 3 of this Annex L.
Likely medical condition: Considering the information within the Passport, it is likely that the Passport is the result of a pathological condition	Inform the *Athlete* via the *ADO* (or send to other Experts).

[Comment: The ABP is a tool to detect the possible Use of Prohibited Substance(s) or Prohibited Method(s) and it is not intended as a health check or for medical monitoring. It is important that the ADO educates the Athletes to ensure that they undergo regular health monitoring and not rely on the ABP for this purpose. Nevertheless, the ADO should inform the Athlete in case the Passport indicates a likely pathology as determined by the Experts.]

L.3 Review by Three Experts

In the event that the evaluation by the appointed Expert in the initial review supports the proposition that the profile, pending other explanation to be provided at a later stage, is likely to be the result the *Use* of a *Prohibited Substance* or *Prohibited Method* and highly unlikely to be the result of a normal physiological or a pathological condition, the Passport shall then be sent for review by the APMU to a group of three Experts, refered to as the Expert panel, composed of the Expert appointed in the initial review and two other Experts. This should take place no later than 7 working days after the reporting of the initial review.

For the review of a Haematological Passport, the Expert panel should have knowledge in the fields of clinical haematology, sport medicine and/or exercise physiology.

For the review of the Steroidal Passport, the Expert panel should be composed of individuals with knowledge in the fields of Laboratory steroid analysis, steroid doping and metabolism and/or clinical endocrinology. In the case of the Steroidal Module, where the first Expert may be from the APMU, the two other Experts must be external to the APMU.

The review by the three Experts must follow the same logic as presented in section 2.2 of this Annex. The three Experts shall each provide their reports in *ADAMS*. This should take place no later than 7 working days after reception of the request.

The APMU is responsible for liaising with the Experts and for advising the *ADO* of the subsequent Expert assessment. If more information is required to review the file, the Experts can request further details, such as those related to medical issues, competition schedule and/or *Sample*(s) analysis details. Such requests are directed via the APMU to the *ADO*.

A unanimous opinion among the three Experts is necessary in order to proceed further towards declaring an *APF*, which means that all three Experts come to the conclusion that considering the available information contained within the Passport at this stage, it is likely that a *Prohibited Substance* or *Prohibited Method* had been used, and highly unlikely that the biological profile is the result of any other cause. The conclusion of the Experts must be reached with the three Experts assessing the *Athlete*'s Passport with the same data (i.e three Expert opinions cannot be accumulated over time, as data is added to a profile).

In the case when two Experts evaluate the Passport as "Likely doping" and the third Expert as "Suspicious" but asking for more information, the APMU can confer with the Expert panel before they finalize their opinion. The group can also seek advice from an appropriate outside Expert, although this must be done with strict confidentiality.

To reach a conclusion in the absence of an *ATPF*, the Expert panel shall come to the unanimous opinion that it is highly likely that the Passport is the result of the *Use* of a *Prohibited Substance* or *Method* and that there is no reasonably conceivable hypothesis under which the Passport might be the result of a physiological condition and highly unlikely that it is the result of pathological condition.

If no unanimity can be reached among the three Experts, the APMU should follow up on requests for additional information or expertise, or recommend the *ADO* to pursue additional *Testing* and/or gather intelligence on the *Athlete* (refer to Information Gathering and Intelligence Sharing Guidelines).

L.4 Compilation of the *ABP* Documentation Package and Joint Expert Evaluation

If the evaluation by the Expert panel supports the proposition that the *Athlete* has likely used a *Prohibited Substance* or *Prohibited Method*, and that the result is highly unlikely due to any another cause, the APMU shall declare a "Likely doping" evaluation in the APMU Report in *ADAMS* and proceed with the compilation of the *ABP* Documentation Package. The APMU may confer with the Expert panel to determine the scope of such compilation, including the recommended elements and the number of tests that need to be included.

[Comment: It is only mandatory to have a full Laboratory Documentation Package for those tests that are deemed essential by the APMU and Expert panel. The other tests, for example those that confirm the baseline levels of a Marker, only require a Certificate of Analysis. A template of the Certificate is available to Laboratories and WADA-Approved Laboratories for the ABP upon request to WADA.]

The following key information needs to be included in both Haematological and Steroidal Modules of the *ABP* Documentation Package:

a) Age of the *Athlete*.
b) Gender of the *Athlete.*
c) Sport and discipline.
d) Type of test (in competition or out of competition).
e) Date of test.
f) *Sample* code number.
g) Internal Laboratory (or *WADA*-Approved Laboratory for the *ABP*) *Sample* number.
h) Biological data and results obtained by the Adaptive Model.
i) *Competition* information.
j) Chain of Custody documentation.
k) Information from the *Doping Control* forms for each *Sample* collected during the period, as determined by the APMU and Expert panel.

For the Haematological Module, the following additional information is required:

l) Information on possible exposure of the *Athlete* to altitude, or altitude simulating devices, for the period defined by the Expert panel.
m) Temperature profile during the transportation of the blood *Sample* and the Blood Stability Score (BSS).
n) Laboratory (or *WADA*-Approved Laboratory for the *ABP*) documentation, including blood results, scattergrams, and internal and external quality controls.
o) Information on whether the *Athlete* received a blood transfusion and/or suffered significant blood loss in the prior three months.

For the Steroidal Module, this additional information is required:

p) pH of the urine *Sample*.
q) Specific gravity of the urine *Sample*.
r) Laboratory documentation, including screening and confirmed (when applicable) values of steroid concentrations and ratios.

s) GC-C-IRMS results, when applicable.

t) Indication of ethanol consumption: urinary concentrations of ethanol and/or ethanol *Metabolites*.

u) Indication of bacterial activities, including 5α-androstandione/A and/or 5β-androstandione/Etio ratio.

v) Indication of medications taken (declared or detected) that may influence the "steroid profile", such as human chorionic gonadotrophin (hCG), ketoconazole, and 5α-reductase inhibitors.

The *ABP* Documentation Package shall be sent by the APMU to the Expert panel, which will review it and provide a joint evaluation to be signed by all three Experts and included in the *ABP* Documentation Package. If necessary, the Expert panel may request complementary information from the APMU.

At this stage, the identity of the *Athlete* is not mentioned but it is accepted that specific information provided may allow to identify the *Athlete*. This shall not affect the validity of the process.

L.5 Issuing an *Adverse Passport Finding (APF)*

If the Expert panel confirms their previous position, considering the information within the Passport at this stage, that it is likely that a *Prohibited Substance or Prohibited Method* had been used, and highly unlikely that it is the result of any other cause, the APMU will issue an *Adverse Passport Finding* (*APF*).

The *APF* represents the end result of the Expert review of the longitudinal profile of *Markers* and other Passport information.

After reviewing the *ABP* Documentation Package, the *ADO* shall:

a) Notify the *Athlete* of the *APF* and inform *WADA* that the *ADO* is considering the assertion of an anti-doping rule violation (ADRV) against the *Athlete*.

b) Provide the *Athlete* and *WADA* the *ABP* Documentation Package.

c) Invite the *Athlete* to provide his/her own explanation, in a timely manner, of the data provided to the *ADO*.

L.6 Review of Explanation from *Athlete*

Upon receipt of any explanation and supporting information from the *Athlete* which should be received within the specified deadline, the APMU shall forward it to the Expert panel for review with any additional information that the Expert panel considers necessary to render its opinion in coordination with both the *ADO* and the APMU. At this stage, the review is no longer anonymous. The Expert panel shall reassess or reassert the case and reach one of the following conclusions:

a. Unanimous opinion of the Experts that based on the information in the Passport, it is likely that the *Athlete* used a *Prohibited Substance* or *Prohibited Method*, and that it is highly unlikely to find the Passport abnormal assuming any other cause; or

b. Based on the available information, the Experts are unable to reach the unanimous opinion set forth above and, in such a case, the Expert panel may or may not recommend further investigation or *Testing*.

L.7 Disciplinary Proceeding

If the Expert panel expresses the opinion set forth in section 6.a., then the *ADO* shall be informed by the APMU and proceed to Results Management (*Code* Article 7.5).

L.8 Passport Re-setting

In the event the *Athlete* has been found to have committed an ADRV based on the Passport, the *Athlete*'s Passport shall be reset at the start of the relevant period of suspension and a new Biological Passport ID shall be assigned in *ADAMS*. This maintains the Athlete's anonymity for potential APMU and Expert panel reviews conducted in the future.

When an *Athlete* is found to have committed an ADRV on any basis other than the *ABP*, the Haematological and/or Steroidal Passport will remain in effect, except in those cases where the *Prohibited Substance* or *Prohibited Method* resulted in an alteration of the haematological or steroidal *Markers*, respectively (e.g. for *AAF* reported for anabolic androgenic steroids, hCG, masking agents or diuretics, which may affect *the Markers* of the "steroid profile," or for the *Use* of Erythropoiesis-Stimulating Agents or blood transfusions, which would alter the haematological *Markers*). In such instances, the *Athlete's* profile(s) would be reset from the time of the beginning of the sanction.

Part Four: Templates

4.0 Scope

A non-mandatory template sharing of information agreement is contained herein to facilitate the sharing and mutual recognition of biological data between *ADOs* that share *ABP* interests on the same *Athlete* (eg. *National Anti-Doping Organization* and *International Federation*).

4.1 Collaboration Agreement

Between

[•]

(hereinafter referred to as "[A]")

and

[•]

(hereinafter referred to as "[B]")

WHEREAS [A] is the [*Anti-Doping Organization* (*ADO*)] recognized by the World Anti-Doping Agency (*WADA*) and is responsible for *Doping Control* and *Athlete Biological Passport* (*ABP*) Programs for *Athletes* included in its *Registered Testing Pool (RTP)*;

WHEREAS [B] is the [*ADO*] recognized by *WADA* and is responsible for *Doping Control* and *ABP* Programs for *Athletes* included in its *RTP*;

WHEREAS the principle of the *ABP* is to have one and only *Passport* for each *Athlete*;

WHEREAS it is therefore of utmost importance that organizations that test the same *Athlete* collaborate to ensure that only one organization consolidate all result for a single *Athlete* and ensure result management of this *Athlete Passport*;

WHEREAS [A] and [B] now wish to collaborate on the planning, *Testing* and results management of the *Doping Control* and *ABP* Programs of the *Athletes* included in their respective *RTPs*, in accordance with the terms of this Agreement.

PURPOSE

The purpose of this Agreement is to provide a framework for collaboration between [A] and [B] (each a Party and collectively the Parties) in relation to the collection and exchange of *Athletes' Passports* and related results management procedures.

THEREFORE, it is agreed upon between the Parties:

Clause 1 - Definitions

Capitalized and italicized terms used in this Agreement shall have the meanings ascribed to them under the World Anti-Doping Code ("*Code*") and the *International Standards*, both as amended from time to time. For ease of reference, relevant definitions have been reproduced in Schedule 1 attached hereto.

Additional definitions created for the purposes of this Agreement shall be underlined and have the following meanings:

1.1 "Agreement" means this Collaboration Agreement.

1.2 "Passport Purposes" means the gathering and collation of *Passports* according to the *ABP* Operating Guidelines and related Technical Documents (TDs).

1.3 "Confidential Information" means all information (however recorded or preserved) disclosed by a Party or its Representatives to the other Party and that Party's Representatives after the date of this Agreement concerning:

(a) the existence and terms of this Agreement;

(b) any information that would be regarded as confidential by a reasonable business person relating to:

(i) the business, affairs, customers, clients, suppliers or future plans of the disclosing Party; or

(ii) the operations, processes, product information, know-how, designs, trade secrets or software of the disclosing Party; and

(c) any information collected, developed or exchanged by the *Parties* in the course of carrying out this Agreement, including, but not limited to, *Passports* and other relevant or potentially relevant doping-related information.

1.4 "Operating Guidelines" means the most recent version of the *ABP* Operating Guidelines adopted by *WADA* and available on *WADA's* Web site.

1.5 "Representative" means an employee, officer, representative, agent or adviser of a Party.

Clause 2 – *Passport Testing* and Information Sharing

2.1 [A] and [B] agree to provide each other with a copy of its updated *RTP* for *Passport* Purposes upon request and to discuss the composition of the respective [A] and [B] *RTP*s where appropriate, in particular when [A] and [B] have *Testing* jurisdiction over the same *Athlete.*

2.2 [A] shall conduct *Testing* of the *Athletes* in [A]'s *RTP* for *Passport* Purposes and [B] shall conduct *Testing* of *Athletes* in [B]'s *RTP* for *Passport* Purposes, including by means of *Target Testing*. For such purposes:

2.2.1 [A] or [A] APMU and [B] or [B] APMU may share intelligence with each other as regards the *Target Testing* of *Athletes* on [A]'s *RTP* or [B]'s *RTP*, as the case may be.

2.2.2 [A] and [B] shall each ensure that it has *Testing* jurisdiction with regard to the tests conducted under this Agreement.

2.2.3 For the avoidance of doubt, nothing in this Clause 2 shall prevent [A] or [B] from *Testing* any *Athlete* within its jurisdiction for *Passport* Purposes at any time, irrespective of the *Athlete's* status on [A]'s *RTP* for *Passport* Purposes or [B]'s *RTP* for *Passport* Purposes.

2.2.4 All *Samples* under this Agreement will be collected in compliance with the International Standard for Testing, the International Standard for Laboratories, and the Operating Guidelines.

2.2.5 [A] and [B] shall each bear its own costs of *Testing* (including the costs of storage, transportation and analysis of *Samples*).

2.3 Each Party agrees that it shall, at its own cost, exclusively use *ADAMS*, and ask the relevant APMU to use *ADAMS*, for recording doping control forms and *Passports* relating to any *Athlete* tested for *Passport* Purposes under this Agreement.

2.4 In any case where an *Athlete* has been tested under this Agreement for *Passport* Purposes, the relevant Party shall record the *Passport* on *ADAMS*, or ensure that it is being recorded by the relevant APMU, as soon as reasonably practical following the test and shall take whatever steps are necessary to ensure that the other Party is able to access the relevant *Passport* through *ADAMS*. If for whatever reason the *Passport* cannot be accessed by the other Party through *ADAMS*, the Party shall provide the relevant *Passport* to the other Party in such other form as the other Party may reasonably request.

2.5 [A] and [B] shall use the *Passports* under this Agreement for *Passport* Purposes only. The relevant *Testing* Authority in each case shall ensure that the *Athlete*'s prior written consent has been obtained for the sharing of the *Passports* with the other Party for such purposes.

Clause 3 – *Passport* Results Management Process

3.1 For each *Athlete* included in both [A] and [B] *RTPs*, the Parties shall establish which of [A] or [B] is the *Passport* Custodian.

3.2 The APMU of the *Passport* Custodian is responsible for results management in accordance with the most recent TD on Result Management Requirements for the *ABP* adopted by *WADA*. For *Athletes* included in both [A] and [B] *RTPs*, *Passports* shall be reviewed after each test by the APMU of the *Passport* Custodian independently of if [A] or [B] was the *Testing* Authority that conducted the last test.

3.3 In *ADAMS*, the Party assigned as the *Passport* Custodian may share the *Athlete's Passport* with the other Party, including the APMU report, targeting recommendations and Expert reviews.

3.4 The Parties have established an Expert panel ([A] Expert panel and [B] Expert panel respectively) working with respectively [A] APMU or [B] APMU in accordance with the Operating Guidelines. Parties shall determine the members of their *ABP* Expert panel from time to time, and shall notify each other upon request of an updated list of their *ABP* Expert panel.

3.5 Parties shall immediately notify each other in writing of the referral of any *Athlete*'s case for review by the other Party's *ABP* Expert panel in accordance with the Operating Guidelines, as well as the outcome of such review.

3.6 For the avoidance of doubt, *Passport* data collected under this Agreement by [A] and [B] should, whenever possible, be combined for the purposes of pursuing a potential anti-doping rule violation (ADRV) or other results management procedure pursued against an *Athlete* in accordance with the *Code* and *International Standards*.

Clause 4 – *Passport* Disciplinary Procedures

4.1 If upon review the [A] *ABP* Expert panel or [B] *ABP* Expert panel (as appropriate) decides that there is no known reasonable explanation for the profile information contained in the *Passport* other than the use by the *Athlete* of a *Prohibited Substance* or *Prohibited Method*, the *Athlete*'s case shall proceed as an asserted ADRV.

4.2 Where the *Passport* Custodian Party decides not to proceed with an asserted ADRV, such decision will not affect the ability of the other Party or *WADA* to appeal such decision.

Clause 5 – Effective Date and Termination

5.1 This Agreement shall become effective on the date of signature and will remain in effect until terminated.

5.2 Notwithstanding Clause 5.3, if either Party wishes to terminate this Agreement, it shall give thirty (30) days' written notice to the other Party of its intention to terminate the Agreement. Upon receipt of the written notice of termination, this Agreement will terminate thirty (30) days after such notice is delivered.

5.3 Either Party may terminate this Agreement immediately if the other Party commits a material breach of any term of this Agreement and (if such breach is remediable) fails to remedy that breach within a period of thirty (30) days after being notified in writing of the breach.

5.4 The Parties agree that after the effective date of termination of this Agreement each Party may continue to use all *Passports* and Confidential Information provided to it by the other Party, provided that it is only used for anti-doping purposes and for a period up to, but not exceeding, the statute of limitations of the *Code* then in force (currently 8 years). The Parties will thereafter, upon request, return, destroy, aggregate or anonymize all *Passports* and Confidential Information in its control or possession provided to it by the other Party, unless applicable law or other applicable regulations prevents the Party from returning or destroying all or part of the *Passports* or Confidential Information.

Clause 6 – Authority

6.1. The Parties hereby represent that they have the full power and authority to enter into and perform this Agreement, and the Parties know of no agreement, promises, or undertakings that would prevent the full execution and performance of this Agreement.

6.2. Notwithstanding the above and for the avoidance of doubt, the Parties acknowledge and agree that nothing in this Agreement affects or modifies their respective rights and obligations, and those of other relevant Third Parties, under the "Agreement Governing the Use and Sharing of Information in *ADAMS*" that the Parties entered into with *WADA*.

Clause 7 - Indemnity

Each Party (the "Breaching Party") shall indemnify and hold harmless the other Party (the "Non-Breaching Party") against any and all costs, charges, damages, expenses and losses (including costs incurred in recovering same) that are incurred by the Non-Breaching Party as a result of any breach of this Agreement by the Breaching Party up to a maximum of [•]. The provisions of this Clause 8 shall survive termination of this Agreement.

Clause 8 – Confidentiality

8.1 The Parties shall at all times keep confidential (and ensure that their Representatives keep confidential) any Confidential Information which they may acquire in accordance with this Agreement and shall not disclose or use such Confidential Information other than in fulfillment of the Agreement except:

(i) with the consent of the other Party; or

(ii) if such information has come into the public domain otherwise than by breach by that Party of this clause; or

(iii) as required by law or other applicable regulations.

8.2. The duties of the Parties in this Clause 8 shall survive the expiration or earlier termination of this Agreement.

8.3. The receiving Party agrees that it will only disclose the disclosing Party's Confidential Information to its directors, employees, consultants or professional advisors on a strictly need-to-know basis in connection with *Passport* Purposes and then only after such person has been advised of the requirements of this Agreement.

Clause 9 – Data Privacy

9.1 The Parties acknowledge that the sharing of Personal Information under this Agreement is necessary to allow each Party to fulfill its obligations under the *Code* and is in accordance with applicable data protection laws.

9.2 The Parties shall collect, Process, store and disclose all Personal Information under this Agreement with the *Athlete*'s consent and in accordance with the International Standard for the Protection of Privacy and Personal Information (ISPPPI).

9.3 Each Party shall notify the other Party promptly of any accidental, unauthorized, or unlawful destruction, loss, alteration, or disclosure of, or access to, the Personal Information ("Security Breach"), and take immediate steps to rectify any Security Breach.

9.4 Neither Party shall disclose *Passports* collected under this Agreement to any Third Party (save for the purposes of the [A] *ABP* Expert panel or [B] *ABP* Expert panel review), without the express prior written consent of the other Party unless such disclosure is required by law or occurs as a result of Clause 9.2.

Clause 10 – Miscellaneous

10.1 This Agreement is intended to be the sole and complete statement of obligation of the Parties as to the subject matter hereof, and supersedes all previous agreements, understandings, negotiations and proposals as to such subject matter.

10.2 The failure of either Party at any time to demand strict performance of the terms of the Agreement shall not be construed as a waiver of the right to demand or receive complete performance of all rights, promises and covenants in this Agreement.

10.3 This Agreement does not establish either Party to be the agent of the other Party or create a joint venture or similar relationship between the Parties and no Party shall have the power to obligate or bind the other Party in any manner whatsoever. The Parties hereto shall act in all respects as independent contractors.

10.4 Neither Party may assign, directly or indirectly, by operation of law, change of control or otherwise, this Agreement or any of its rights and obligations hereunder, without the prior written consent of the other Party, which shall not be unreasonably withheld.

10.5 The Parties agree that any and all amendments to this Agreement must be made in writing to be signed by the Parties; no amendment can be made by electronic means.

10.6 If any provision or provisions of this Agreement shall be held to be invalid, illegal, or unenforceable, such provision shall be enforced to the fullest extent permitted by applicable law and the validity, legality, and enforceability of the remaining provisions shall not in any way be affected or impaired thereby.

10.7 A *Person* who is not a party to this Agreement shall not have any rights under or in connection with this Agreement. The rights of the Parties to terminate, rescind or agree any variation, waiver or settlement under this Agreement are not subject to the consent of any person that is not a party to this Agreement.

10.8 Section and other headings in this Agreement are for convenience of reference only and shall not constitute a part of or otherwise affect the meaning or interpretation of this Agreement.

Clause 11 - Notices

11.1 Any notice required to be given under this Agreement shall be in writing and shall be delivered personally, sent by fax or sent by commercial courier, to the other Party required to receive the notice at its address as set out below:

(i) [A]:

Address: [•]
For the attention of: [•]
Fax number: [•]

(ii) [B]:

Address: [•]
For the attention of: [•]
Fax number: [•]

or at such other address as the relevant Party may specify by notice in writing to the other Party.

11.2 Any notice shall be deemed to have been duly given:

(a) if delivered personally, at the time of delivery at the address referred to in Clause 12.1;

(b) if delivered by commercial courier, at the time of signature of the courier's receipt; or

(c) if sent by fax, at the time of transmission.

Clause 12 – Applicable Law and Jurisdiction

12.1 This Agreement and any dispute or claim arising out of or in connection with it or its subject matter shall be governed by and construed in accordance with the law of [•].

12.2 Both Parties accept and agree to comply with any relevant and applicable laws and regulations.

12.3 The Parties agree that any dispute, arguments or claims arising with respect to or in connection with the execution of this Agreement (as well as any subsequent amendment hereof, including, for example, its structure, validity, effectiveness, interpretation,

execution, infringement or termination, and also any non-contractual claim relating hereto) shall be the object of an amicable resolution. In the absence of amicable resolution, the dispute shall be submitted to the exclusive jurisdiction of the Court of Arbitration for Sport (*CAS*) in Lausanne, Switzerland, and settled definitively in accordance with the Code of Sports-related Arbitration. The panel will consist of one arbitrator. The language of the arbitration will be [•].

Clause 13 - Signatories

The signatories to this Agreement hereby warrant that they have read and agree to the terms, conditions and provisions of this Agreement, including any Appendices, and have full power and authority to sign for and bind their respective organizations.

Clause 14 - Counterparts

This Agreement may be executed in any number of counterparts, each of which shall be deemed an original but all of which shall constitute one and the same instrument.

In the name and on behalf of
[A]

_____

……..[Name, Position]

Date: _____

In the name and on behalf of
[B]

_____

……..[Name, Position]

Date: _____